AANP | American Association of NURSE PRACTITIONERS®

The Essential Pocket Guide to

Opioid Use Disorder

About This Guide

As the opioid epidemic continues to surge across the country, the American Association of Nurse Practitioners® (AANP) developed this pocket guide as a reference tool designed to provide easy access when you need it. This guide is intended to provide information regarding disease state, symptoms, and treatments of this chronic, relapsing disease of the brain. This guide is also available through the AANP mobile application and as a mobile-friendly website.

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Key Terms

- **Addiction**: a primary, chronic relapsing disease of brain reward, motivation, memory, and related circuitry characterized by inability to consistently abstain, impairment in behavioral control, craving, diminished recognition of significant problems with one's behaviors and interpersonal relationships, and a dysfunctional emotional response. Like other chronic diseases, addiction often involves cycles of relapse and remission.
- **Medically supervised withdrawal** (formerly called detoxification): Using an opioid agonist (or an alpha-2 adrenergic agonist) in tapering doses or other medications to help a patient discontinue illicit or prescription opioids.
- **MOUD**: Medications for opioid use disorder
- **Opioid misuse**: The use of prescription opioids in any way other than as directed by a prescriber; the use of any opioid in a manner, situation, amount, or frequency that can cause harm to self or others.
- **Opioid receptor agonist**: a substance that has an affinity for and stimulates physiological activity at cell receptors in the central nervous system (CNS) that are normally stimulated by opioids.
- **Opioid receptor antagonist**: A substance that has affinity for opioid receptors in the CNS without producing the physiological effects of opioid agonists.
- **Opioids**: All natural, synthetic, and semisynthetic substances that have effects similar to morphine.
- **Opioid treatment program (OTP)**: An accredited treatment program with SAMHSA certification and DEA registration to administer and dispense MOUD approved by FDA to treat opioid addiction.

Source: Substance Abuse and Mental Health Services Administration (SAMHSA). TIP 63: Medications for Opioid Use Disorder. 2021. https://www.samhsa.gov/resource/ebp/tip-63-medications-opioid-use-disorder.

- **Opioid use disorder (OUD)**: Per DSM-5, a disorder characterized by loss of control of opioid use, risky opioid use, impaired social functioning, tolerance, and withdrawal.
- **Recovery**: A process of change through which individuals improve their health and wellness, live self-directed lives, and strive to reach their full potential.
- **Relapse**: A process in which a person with OUD who has been in remission experiences a return of symptoms or loss of remission. A relapse is different from a return to opioid use in that it involves more than a single incident of use. Relapses occur over a period of time and can be interrupted. Relapse need not be long lasting.
- **Remission**: DSM-5 defines remission as present in people who previously met OUD criteria but no longer meet any OUD criteria (with the possible exception of craving). Remission is an essential element of recovery. Notably, remission does not have to be abstinence. The individual can be in remission while using MOUD
- **Return to opioid use**: One or more instances of opioid misuse without a return of symptoms of OUD. A return to opioid use may lead to relapse.
- **Tolerance**: Alteration of the body's responsiveness to alcohol or other drugs (including opioids) such that higher doses are required to produce the same effect achieved during initial use.

Introduction

In 2019, 10.1 million Americans ages 12 and older (3.7% of the population) reported misusing opioids in the past year, and of those, 9.7 million misused prescription pain relievers and 745,000 used heroin.[1] Although initially driven by the activation of reward centers in the brain, chronic opioid use increasingly engages anti-reward mechanisms that drive adverse emotional states, leading to increased use and eventual relapse in those who try to quit.[2] Since 1999, the age-adjusted mortality rate from drug overdose has tripled and two-thirds of the more than 760,000 drug overdose deaths have involved an opioid.[3]

Opioid use disorder (OUD), defined by the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) as a problematic pattern of opioid use leading to problems or distress,[4] is an important public health issue given the potential addictiveness of opioids, the extent of associated harm, and the impacts of drug-use behaviors, such as HIV and Hep C infections and transmission, bacterial endocarditis, and neonatal abstinence syndrome. Societal costs associated with OUD include harm to family cohesion, reduced employment and economic contribution, and increased risks and costs of crime.[2]

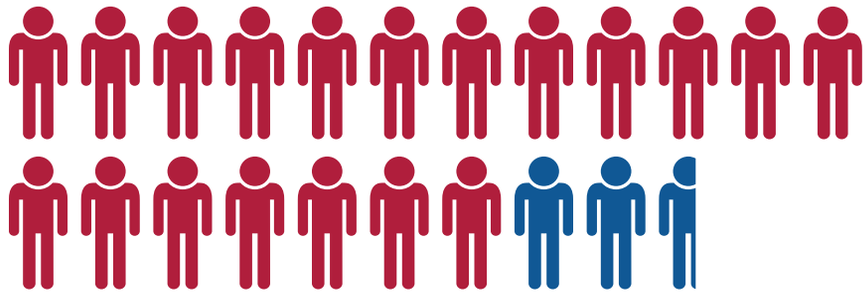
A survey by the American Hospital Association found that one-third of respondents knew someone with OUD;[6] despite the ubiquity and scope of this public health problem, the medical community's understanding of OUD has been complicated by strong public and political opinions about drug use behaviors.[2,7] Providers have reported concerns regarding diversion with prescribing medications for OUD, thus delaying care while patients await referral.[7] Negative stigma about people with OUD and medical treatment for the disorder continues to negatively impact patient health outcomes. In 2019, 21.6 million Americans needed treatment for substance use disorder (SUD), which includes OUD, but only 2.6 million (12%) received treatment.[1]

10.1 million
people misused prescription opioids in the past year[5]

96,779
people died from drug overdose from 3/2020 to 3/2021 (**36.1% more than in 2019**)[5a]

1.6 million
people had OUD[5]

In 2019, **21.6 million** Americans **needed treatment**...



But only **2.6 million** received any.[1]

According to the National Institute on Drug Abuse (NIDA), "scientific research has established that medication-assisted treatment of opioid addiction increases patient retention and decreases drug use, infectious disease transmission, and criminal activity." Research confirms that medical treatment is life-extending for individuals with OUD.[8]

This Pocket Guide provides a review of the current evidence-based screening, diagnosis, and medical treatment of OUD in a portable format that may easily be referenced during clinical practice, with a goal of improving the lives of people suffering from OUD.

This means **~7 out of every 8 people go untreated.**

How Did We Get Here?

1980 The **HIV epidemic draws attention to untreated pain.**

An expert opinion article, paid for by pharmaceutical companies selling opioids, is published stating **"addiction is rare for patients treated with narcotics."** It's been cited more than 600 times and was **grossly misrepresented more than 80% of the time** because it only applied to acute therapy in the hospital setting, not long-term use.

"Pain is a more terrible lord of mankind than even death itself." - Albert Schweitzer, physician, 1875-1965

1990 A multitude of literature is published about **under-treatment of pain.**

"If we know that severe pain and suffering can be alleviated, and do nothing about it, then we ourselves become the tormentors."

- Primo Levi, chemist, Auschwitz survivor, 1919-1987

1996 The American Pain Society **declares pain the fifth vital sign.**

Oxycontin receives FDA approval.

1998 The OxyContin manufacturer releases a **huge marketing push.**

Timeline[9]

TODAY Many new programs and guidelines have been put into place to regulate opioids.

Drug addiction rehabilitation receives more funding.

2017 **17% of Americans have at least one opioid prescription,** and more than **11.4 million people ages 12 and older misuse opioids.**

2016 **64,000 people die** from opioid overdoses.

2010 Prescription use of opioids is **increasing.**

2007 The **manufacturer is found guilty** of criminal charges for misleading the public and healthcare workers on the addictive properties of OxyContin.

2000 The Joint Commission establishes assessment and intervention requirements in pain management.

"Nobody will laugh long who deals much with opium: its pleasures even are of a grave and solemn complexion."[3]

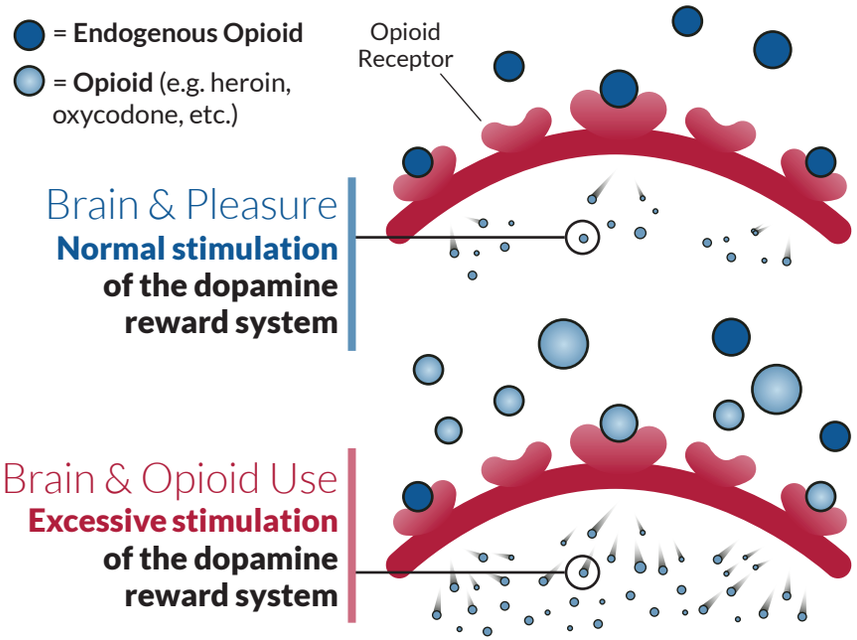
- Thomas de Quincy, writer, 1785-1859

The Neurobiology of OUD

The endogenous opioid system is a complex neuromodulatory system composed of endogenous opioid peptides (β-endorphins, enkephalins, and dynorphins) and their receptors (mu [μ] opioid receptors, delta [δ], and kappa [κ], respectively).[2] Opioids act on these receptors with varying potency, efficacy, and pharmacokinetics. Both mu and delta opioid receptors mediate the analgesic and rewarding/addictive properties of opioids, whereas kappa opioid receptors have limited clinical analgesic properties due to undesirable effects of dysphoria, anxiety, and hallucinations.[10]

It's important to note that endogenous opioids are expressed naturally throughout the peripheral and central nervous system and regulate many aspects of physiology, including pain processing, stress reactivity, reward sensitivity, mood, respiration, and gastrointestinal, endocrine, and immune functions.[2] Clinically, mu opioid receptor agonists are important analgesics due to their ability to inhibit pain in the dorsal horn of the spinal cord; however, mu opioid receptor agonist drugs are profoundly rewarding to both animals and humans, independent of pain or discomfort.[2,10]

Opioid Receptors & Opioid Use[12]



Heroin, morphine, fentanyl, methadone, codeine, hydrocodone, and oxycodone are full mu opioid receptor agonists, and with repeated use, tolerance occurs and leads to reductions in drug effects (analgesia, reward), requiring higher doses to achieve similar effects.[10,11] Chronic use of opioids also leads to long-lasting alteration of other neurotransmitter systems, such as dopamine, glutamate, and GABA. The impact of opioids on the respiratory system (particularly highly-potent fentanyl) is the underlying cause of overdose deaths due to inhibition of the brainstem respiratory centers, which have abundant mu opioid receptors.[10]

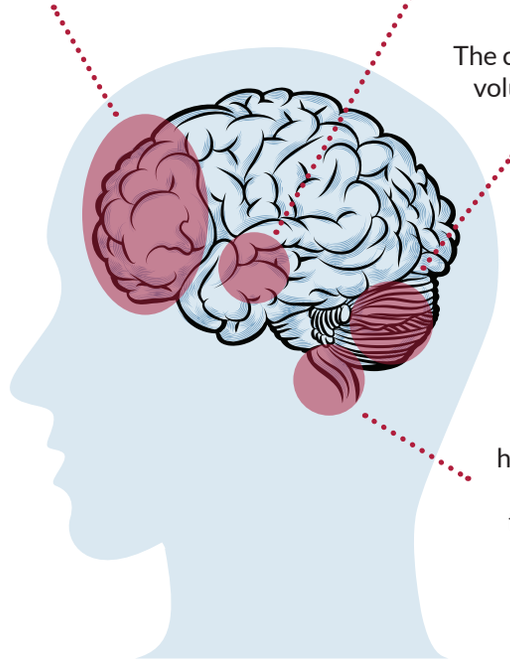
Effects of Opioids on the Brain[13]

Prefrontal Cortex

The prefrontal cortex, which continues to develop in early life, helps form complex thoughts and planning. Opioid use has a significant effect here, disrupting one's ability to make conscious decisions.

Midbrain & Amygdala

The amygdala, located in the midbrain, controls emotions and motivation. It is here that opioids trigger the feeling of pleasure and create urges and cravings, and influence behaviors.



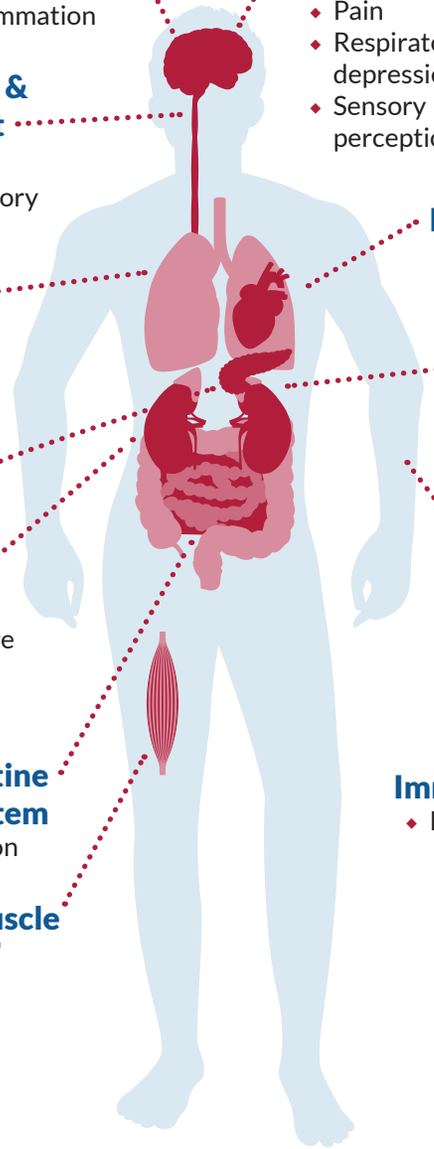
Cerebellum

The cerebellum signals the body's voluntary motor functions, such as balance and coordination. An opioid overdose has shown to cause cerebellar swelling and edema.

Brain Stem

The brain stem controls the body's autonomic functions, like breathing and heart rate. When its functions are suppressed by opioids, the decreased heart rate and respiratory rate can be fatal.

Effect of Opioids on the Body[14]



Brain Microglia
- Neuroinflammation

Brain Neurons
- Feeding
- Pain
- Respiratory depression
- Sensory perception
- Pleasure
- Emotions
- Motivation
- Learning
- Neurogenesis
- Stress

Spinal Cord & Dorsal Root Ganglion
- Pain & sensory perception

Heart
- Cardioprotection
- Heart rate

Lung
- Decrease respiration
- Cancer

Adrenal Gland
- Reduce cortisol
- Affect immune & stress responses

Pancrease
- Weight gain

Skin
- Analgesia
- Anti-inflammation
- Slow wound healing

Kidney
- Renal failure
- Urinary retention

Immune System
- Immunosuppression

Small Intestine Enteric System
- Constipation

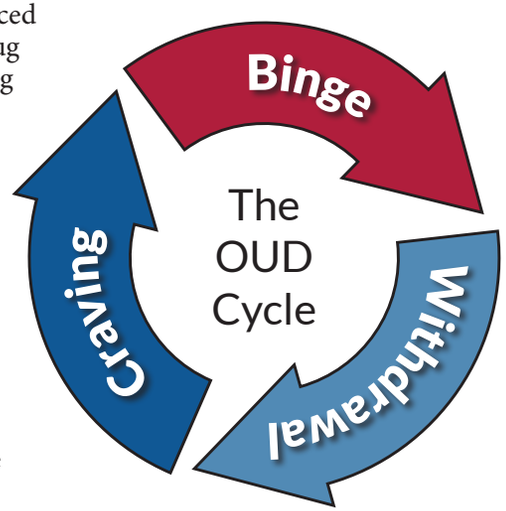
Skeletal Muscle
- "Twitching"
- Weakness

The Cycle of OUD

The impact of chronic opioid use on the brain and body is complex, and a detailed review of these mechanisms is outside the scope of this document. However, understanding the neurobiology and resulting addiction cycle is critical to not only sympathizing with the challenges of living with OUD, but also the important role of medication to break the cycle and achieve sobriety.

Opioid drugs are highly addictive. Animals provided with opioids under restricted conditions maintain stable levels of opioid intake without major signs of physical dependence; however, when animals are provided unlimited access to opioids, their intake rapidly escalates.[2,15,16] Over time, tolerance to opioid analgesia necessitates increasingly higher doses to sustain analgesic effects, and withdrawal from chronic use produces hyperalgesia (lower pain thresholds). Individuals who have used opioids for weeks to years may unexpectedly develop abnormal pain and hyperalgesia upon withdrawal from therapy. In addition, opioids are now thought to have analgesic properties against emotional pain, and this is a key behavioral mechanism driving the withdrawal/negative affect stage of the addiction cycle.[17]

With chronic opioid use, the endogenous opioid system becomes hijacked, and it has been hypothesized that a three-stage cycle develops.[2] The binge stage involves brain circuits involved in incentivized salience (or importance), which involves increased motivation for the drug produced by cues associated with the drug and pathological habits. During the withdrawal stage, drug absence leads to a negative emotional state due to several mechanisms, such as the loss of reward function in the basal ganglia and activation of averse brain stress systems in the extended amygdala, which mediates negative reward signals. Ultimately, the craving stage leads to deficits in executive functioning in the prefrontal cortex.[2]



The Cycle of OUD

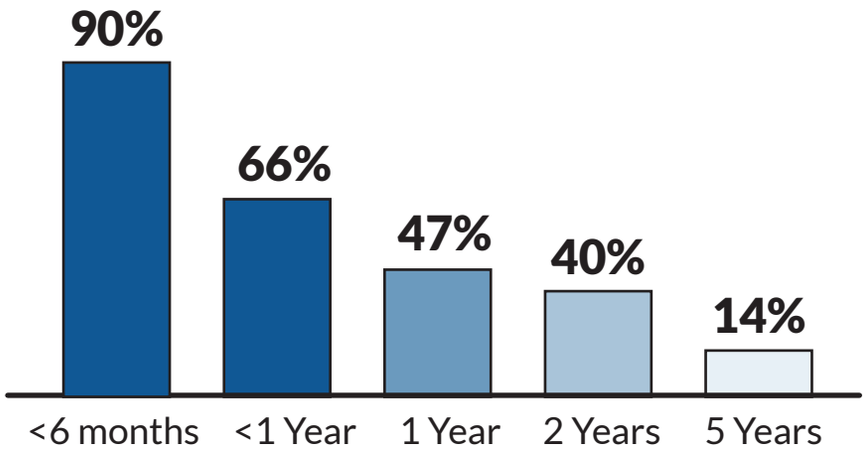
Impairments to cognitive processes, including executive function, information processing speed, verbal learning, and non-verbal learning may remain for years after the acute withdrawal phase has passed.[18] Furthermore, as the result of opioids hijacking the reward system in the brain, individuals who achieve abstinence continue to experience a reward-deficient state in which conventional rewards have lost salience. Impairments in these domains contribute to the poor decision-making that drives drug-seeking and relapse.[11]

The break with emotional homeostasis (or hyperkatifeia, defined as hypersensitivity to emotional distress in the context of opioid abuse) does not end with acute withdrawal and can extend into prolonged abstinence, further adding to the risk of relapse.[17]

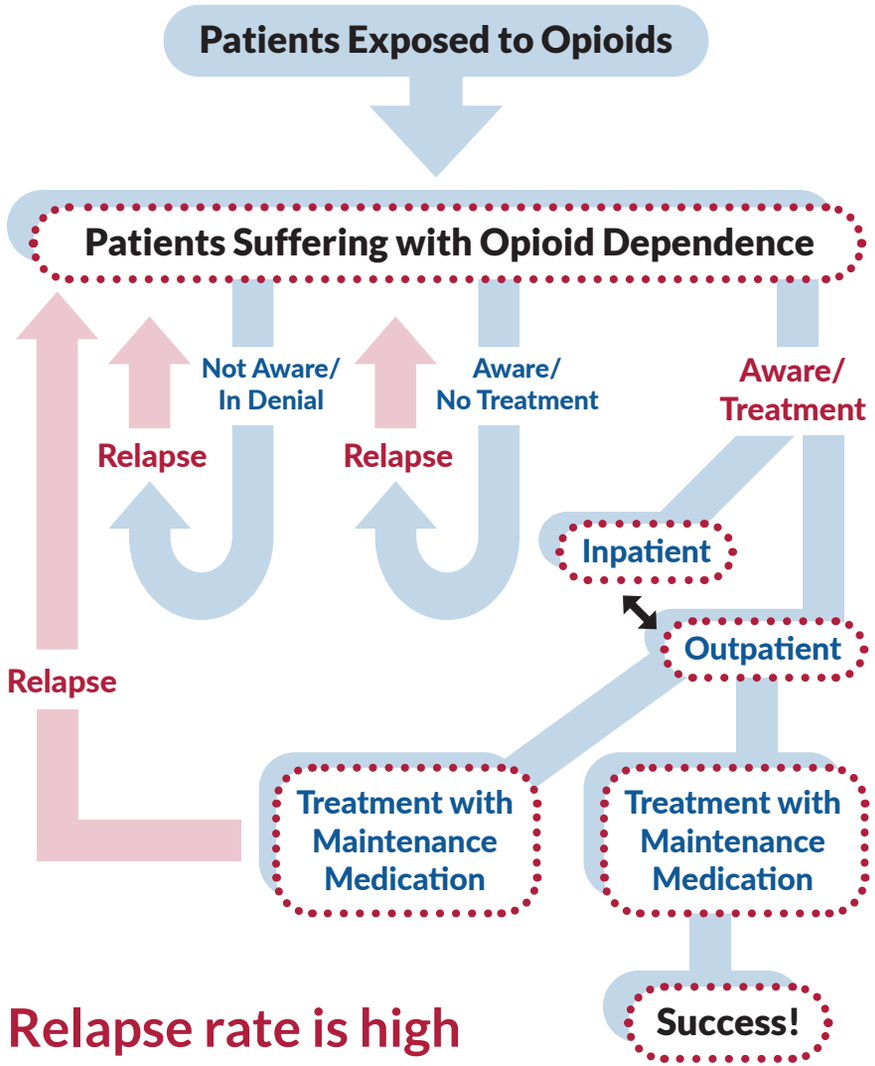
Opioids have also been shown to support conditioned place preference, whereby environmental conditions, such as riding in a car or standing on a street corner, associated with the drug's use can trigger an "expectation of reward" once acute withdrawal has passed.[2]

Collectively, OUD is extremely challenging to successfully overcome. One study found that following discharge from a residential addiction treatment service, 91% of patients who had been dependent on opioids eventually relapsed. Of those who did relapse, 59% did so within one week of discharge, and altogether 80% of patients relapsed within one month of discharge.[19] The identification, diagnosis, and treatment of OUD begins what will be a lifelong journey for patients and their families.

Chance of Relapse Based on Length of Time Abstinent[17,17a]

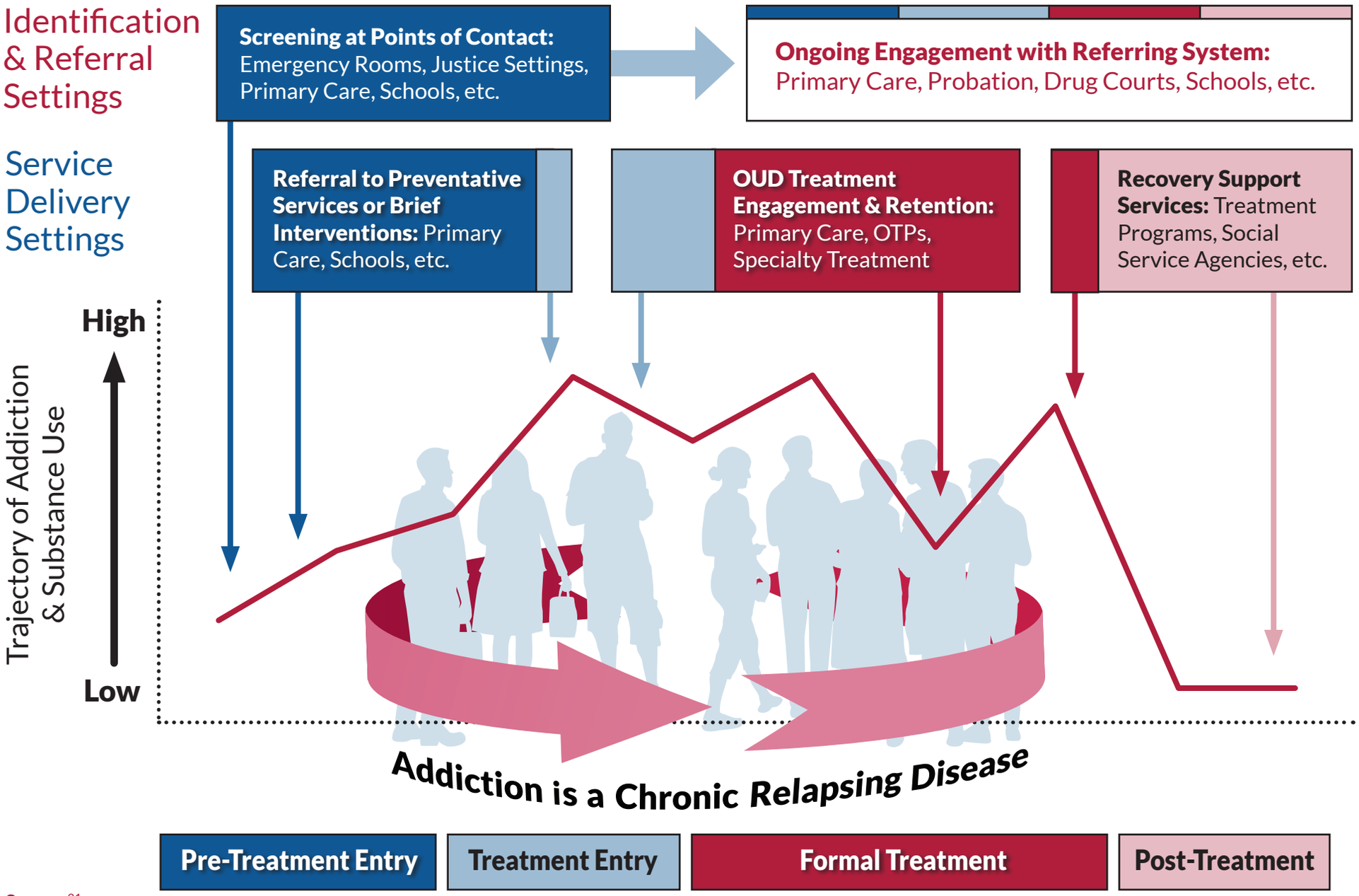


The Journey of OUD Treatment[17]



Relapse rate is high without proper treatment approach.

Opportunities for Intervention



Source[21]

Identifying & Diagnosing OUD

Practically, OUD is best understood as a biopsychosocial disorder in which genetic factors, adverse early development, mental illness, social norms, drug exposure, and market availability can influence the extent of exposure and the opportunity for drug use, as well as the progression and development of OUD and associated harms.[2]

OUD is defined by the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) as a problematic pattern of opioid use leading to problems or distress. DSM-5 criteria for substance use disorder (SUD; including OUD) are shown below.[4]

A substance use disorder is defined as **having 2 or more of the following** in the past year resulting in **distress or impairment**:

Loss of Control

- More than intended
  - Amount used
  - Time spent
- Unable to cut down
- Giving up activities
- Craving

Physiology

- Tolerance
- Withdrawal

formerly "dependence"

Consequences

- Unfulfilled obligations
  - Work
  - School
  - Home
- Interpersonal problems
- Dangerous situations
- Medical problems

formerly "abuse"

Severity is rated by the number of symptoms present

2-3	**Mild**
4-5	**Moderate**
6+	**Severe**

Tolerance and withdrawal alone don't necessarily imply a disorder!

Overview of Screening for OUD

Given the enormous burden on patients, their families, and society, identifying OUD during routine clinical practice is vital. Appropriate substance use screening and brief assessment can:[22]

- Normalize discussions about substance use
- Provide opportunities for prevention by reinforcing healthy behaviors
- Assist providers in diagnosing and treating medical and psychiatric conditions
- Inform prescribing practices to avoid overdose and medication interactions
- Identify patients at risk for problem substance use
- Guide brief interventions and treatment recommendations
- Identify patients in need of treatment for a SUD, such as OUD

NIDA recommends several evidence-based screening tools and assessment resources for patients suspected of drug misuse.[23] Results of screening tools should be used as the start of a productive conversation with the patient about their substance use and strategies to reduce their risk.[22,24–26]

Screening Tools for OUD[22-26]

	Adults	Adolescents	Time
Screening Tools			
TAPS-1 (Tobacco, Alcohol, Prescription medication, and other Substance use)	X		5 min
ORT (Opioid Risk Tool)	X		<1 min
ORT-OUD (Opioid Risk Tool – OUD)	X		<1 min
Assessments			
TAPS-2 (Tobacco, Alcohol, Prescription medication, and other Substance use)	X		5 min
CRAFFT (Car, Relax, Alone, Forget, Friends, Trouble)		X	<1 min

Screening Adults for OUD

Opioid Risk Tool (ORT)

The ORT is a brief, self-reported screening tool that can be administered and scored in less than 1 minute in the primary care setting to assess risk for opioid abuse among those prescribed opioids for chronic pain; however, this tool has not been validated in non-pain patients.[26]

Mark each box that applies	Female	Male
Family history of substance abuse		
Alcohol	1	3
Illegal drugs	2	3
Rx drugs	4	4
Personal history of substance abuse		
Alcohol	3	3
Illegal drugs	4	4
Rx drugs	5	5
Age between 16-45 years	1	1
History of pre-adolescent sexual abuse	3	0
Psychological disease		
ADD, OCD, Bipolar, Schizophrenia	2	2
Depression	1	1
Scoring Totals		

≤3 Low risk for future opioid abuse
4-7 Moderate risk for opioid abuse
≥8 High risk for opioid abuse

ORT-OUD

The ORT-OUD should be administered to patients upon initial clinic visit prior to beginning or continuing opioid therapy for pain. Similar to the ORT, this tool has not been validated in non-pain patients.[25]

Mark each box that applies	Yes	No
Family history of substance abuse		
Alcohol	1	0
Illegal drugs	1	0
Rx drugs	1	0
Personal history of substance abuse		
Alcohol	1	0
Illegal drugs	1	0
Rx drugs	1	0
Age between 16-45 years	1	0
History of pre-adolescent sexual abuse	1	0
Psychological disease		
ADD, OCD, Bipolar, Schizophrenia	1	0
Depression	1	0
Scoring Totals		

≤2 Low risk for future OUD
≥3 High risk for OUD

Screening Adults for OUD

Tobacco, Alcohol, Prescription medication, and other Substance use (TAPS); Available at: https://nida.nih.gov/taps

This tool consists of a screening component (TAPS-1) followed by a brief assessment (TAPS-2) for those who screen positive. **This tool must be administered electronically** and can either be filled out by the patient directly or filled out by the clinician during an interview with the patient. Tool administration should take 5 minutes or less.[22]

Once completed, the TAPS tool will automatically calculate the patient's score. **Patients suspected of opioid misuse should be further assessed with DSM-5 criteria if a 1 or higher is scored on the TAPS tool.**[22]

TAPS Tool Part 1 — *In the past 12 months...*

1. **How often have you used any tobacco product** (e.g. cigarettes, e-cigarettes, cigars, pipe, or smokeless tobacco)?

   ☐ Never ☐ <Monthly ☐ Monthly ☐ Weekly ☐ Daily or almost daily

2. **Males Only: How often have you had 5 or more drinks containing alcohol in 1 day?** One standard drink is about 1 small glass of wine (5 oz), 1 beer (12 oz), or 1 single shot of liquor.

   ☐ Never ☐ <Monthly ☐ Monthly ☐ Weekly ☐ Daily or almost daily

3. **Females Only: How often have you had 4 or more drinks containing alcohol in 1 day?** One standard drink is about 1 small glass of wine (5 oz), 1 beer (12 oz), or 1 single shot of liquor.

   ☐ Never ☐ <Monthly ☐ Monthly ☐ Weekly ☐ Daily or almost daily

4. **How often have you used any drugs** including marijuana, cocaine or crack, heroin, methamphetamine (crystal meth), hallucinogens, or ecstasy/MDMA?

   ☐ Never ☐ <Monthly ☐ Monthly ☐ Weekly ☐ Daily or almost daily

5. **How often have you used any prescription medications just for the feeling, more than prescribed, or that were not prescribed for you?** Prescription medications that may be used this way include opiate pain relievers (e.g. OxyContin, Vicodin, Percocet, or methadone), medications for anxiety or sleeping (e.g. Xanax, Ativan, or Klonopin), or medications for ADHD (e.g. Adderall or Ritalin).

   ☐ Never ☐ <Monthly ☐ Monthly ☐ Weekly ☐ Daily or almost daily

A key strength of the TAPS tool is that it may be used in any adult patients, not just those starting or continuing pain therapy.

A more in-depth Part 2 (examines past 3 months and is not included herein) will automatically continue on the website depending on the patient's responses.

Score must be calculated electronically

0	**No use in past 3 months**
1	**Problem use**
2+	**Higher risk**

Screening Adolescents for OUD

CRAFFT Interview v2.1[24]

Available at: http://crafft.org/get-the-crafft/

The CRAFFT is a well-validated substance use screening tool for adolescents ages 12-21 and recommended by the American Academy of Pediatrics' Bright Futures Guidelines for preventive care screenings and well-visits.[24]

Begin: "*I'm going to ask you a few questions that I ask all my patients. Please be honest. I will keep your answers confidential.*"

During the past 12 months, on how many days did you:

1. Drink more than a few sips of beer, wine, or any drink containing **alcohol**? Say "0" if none.
2. Use any **marijuana** (cannabis, weed, oil, wax, or hash by smoking, vaping, dabbing, or in edibles) or "**synthetic marijuana**" (like "K2", "Spice")? Say "0" if none.
3. Use **anything else to get high** (like other illegal drugs, pills, prescription or over-the-counter medications, and things that you sniff, huff, vape, or inject)**?** Say "0" if none.

Did the patient answer "0" for all questions above?

Yes → Ask **CAR** question only

No → ***CRAFFT** Screen

*Two or more YES answers on the CRAFFT screen (opposite page) suggest a serious problem and a need for further assessment.

C Have you ever ridden in a **CAR** driven by someone (including yourself) who was "high" or had been using alcohol or drugs?

R Do you ever use alcohol or drugs to **RELAX**, feel better about yourself, or fit in?

A Do you ever use alcohol or drugs while you are by yourself, or **ALONE**?

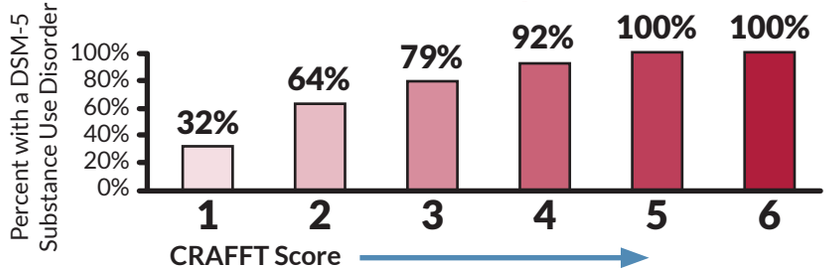
F Do you ever **FORGET** things you did while using alcohol or drugs?

F Do your **FAMILY** or **FRIENDS** ever tell you that you should cut down on your drinking or drug use?

T Have you ever gotten into **TROUBLE** while you were using alcohol or drugs?

Discuss level of risk and potential interventions for substance use disorder.

CRAFFT Score Interpretation



Communication Skills

When OUD is suspected, patients should be approached with compassion using relationship-building skills. Example phrases include:[27]

- *"Sometimes the medications cause problems that we cannot anticipate."*
- *"All kinds of people have problems with opioids."*
- *"You are not alone. All kinds of people can have problems with opioids."*
- *"I understand you have been struggling and know that discussing change can be distressing."*
- *"My primary motivation is to provide care that leads to the healthiest version of 'you' in the long term."*
- *"Getting help for this is like getting help for any other chronic medical problem."*
- *"I want you to have the best possible care, and this difficult but productive conversation is a first step for us."*

Motivational interviewing is a conversational method for talking with your patients about several health issues, including substance use. Based on a high level of evidence, it is a strategy to help engage individuals in making a change in their behaviors. The acronym OARS describes the four core skills of motivational interviewing: open questions (O); affirmations (A); reflective listening (R); and summarizing (S).[28]

The OARS Model includes four basic skills:

O = Open Questions

A = Affirmations

R = Reflective Listening

S = Summarizing

Open Questions[29]

- Establish a safe environment, and build trusting and respectful relationship.
- Explore, clarify, and gain an understanding of your patient's world.
- Learn about the patient's past experience, feelings, thoughts, beliefs, and behaviors.
- Gather information – patient does most of the talking.
- Help the patient make an informed decision.

Helpful Tip:

1. Avoid asking "why" (asks patients to justify a decision/ behavior) and instead ask "how" or "what" (seeking to understand).

Affirmations[29]

- Build rapport; demonstrate empathy; affirm exploration into the patient's world.
- Affirm the patient's past decisions, abilities, and healthy behaviors.
- Build a patient's self-efficacy – an ability to believe they can be responsible for their own decisions and their lives.

Helpful Tips:

1. Use appropriate silence, attentive body posture, and appropriate eye contact.
2. Maintain relaxed facial expression and voice tone.
3. Use statements of appreciation, understanding, and positive feedback.

Reflective Listening[29]

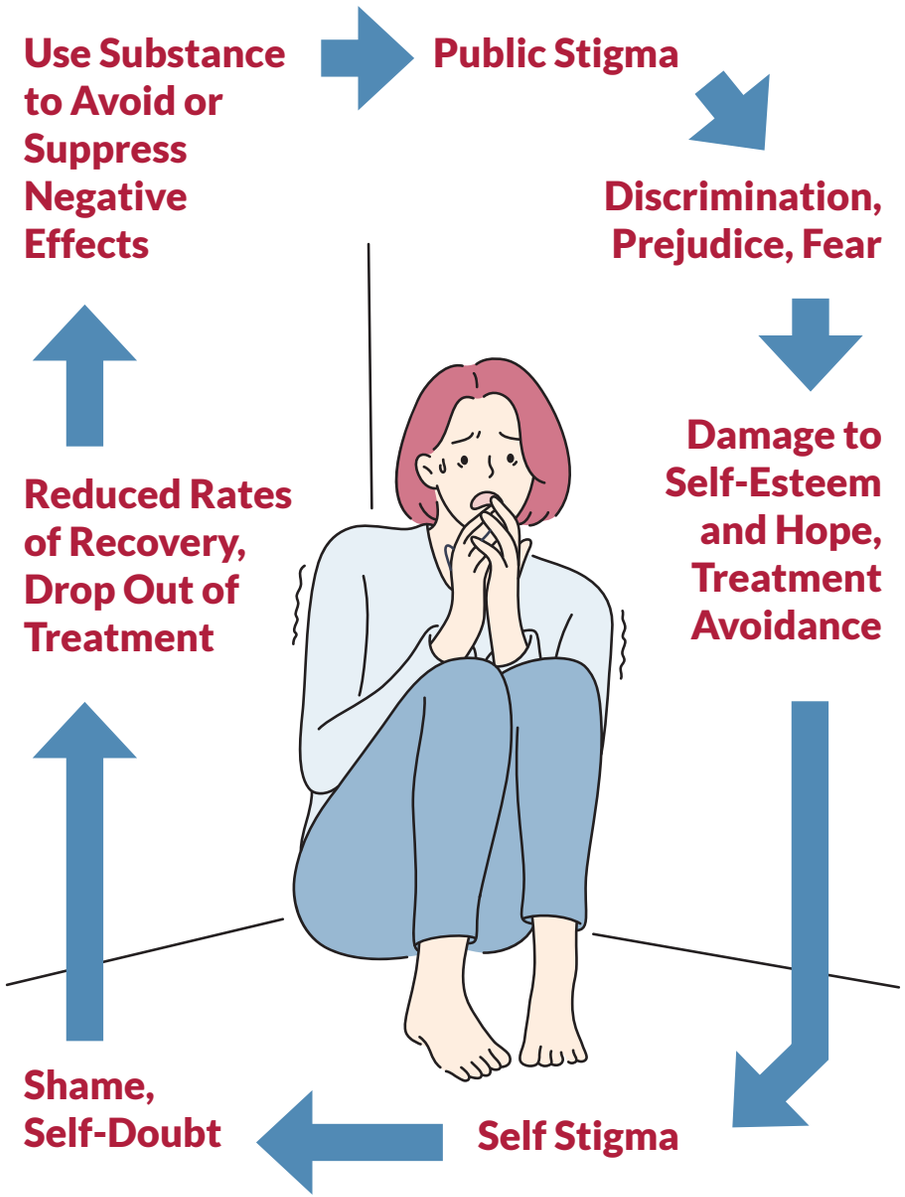
- Demonstrate to the patient that you are listening and trying to understand his/her situation.
- Offer the patient an opportunity to "hear" his/ her own words, feelings and behaviors reflected back to him/her.
- Reflect the patient's thoughts, feelings, and behaviors.
- Reflect the patient's general experiences and the "in the moment" experience of the clinic visit.

Summarizing[29]

The goal of summarizing is to transition and close the conversation. Three variations of summarizing are:

1. **Collective Summary:** "So let's go over what we have talked about so far."
2. **Linking Summary:** "A minute ago you said you wanted to talk to…Maybe now we can talk about how you might try…"
3. **Transitional Summary:** "So you will make an appointment today before you leave and I will see you again soon."

Break the Cycle of Stigma



Source[30–32]

Assessment Following Screening

Patients should be assessed for OUD if they screen positive for opioid use, disclose opioid use or show signs/symptoms of opioid misuse.[33] Signs and symptoms of opioid misuse are shown below.

Intoxication Signs	Withdrawal Signs
Drooping eyelids Constricted pupils Reduced respiratory rate Scratching (due to histamine release) Head nodding	Restlessness, irritability, anxiety Insomnia Yawning Abdominal cramps, diarrhea, vomiting Dilated pupils Sweating Piloerection

The extent of assessment should depend on the provider's ability to treat patients directly. ***If the provider does not offer medical treatment***, the focus should be on the following:[33]

- Medical assessment
- Making diagnosis of OUD
- Patient safety
- Comorbidity assessment and management
- Motivational brief interventions to promote safer behavior and foster effective treatment engagement
- Overdose prevention education and provide a naloxone prescription.
- Education for patients who inject drugs on how to access sterile injecting equipment.
- An in-person follow-up, regardless of referral to specialty treatment

If the provider does offer medical treatment, a more comprehensive assessment is warranted and should also include:[33]

- A review of the prescription drug monitoring program (PDMP)
- A history, including a review of systems
- A targeted physical exam for signs of opioid withdrawal, intoxication, injection, and other medical consequences of misuse
- Determination of OUD diagnosis and severity
- Appropriate laboratory tests in addition to those recommended by the non-treating provider

Lab Checklist

When OUD is suspected or diagnosed, the following laboratory tests should be conducted:[27,33]

- Test urine for opioids, alcohol (ethyl glucuronide), and other drugs, such as benzodiazepines
- Opioid testing should include basic opiates (morphine, codeine, heroin), expanded opiates (oxycodone & hydrocodone), tramadol, methadone, buprenorphine & its metabolites, and fentanyl (via blood is best)
- Conduct a complete blood count (especially if any signs of bacterial infection such as endocarditis)
- Assess for hepatitis B/C and HIV for those who inject intravenously
- Offer vaccination for patients who inject drugs and have negative hepatitis B serology
- Consider testing for syphilis and tuberculosis if indicated
- Assess liver and kidney function with liver enzymes, serum bilirubin, and serum creatinine blood tests
- All women of childbearing age should receive a pregnancy test

Urine Drug Testing Window of Detection[33]

Drug	Detection Window	Comments & Potential False Positives
Amphetamine; methamphetamine; 3-4-methylenedioxy-methamphetamine	1-4 days	**Potential false positives**: chlorpromazine, antihistamines, phenylpropanolamine, bupropion, & ranitidine. Confirm unexpected positive with lab.
Barbiturates	<6 weeks	Ibuprofen & naproxen
Benzodiazepines	1-3 days; <6 weeks if heavy chronic use	Immunoassays may not be sensitive to therapeutic doses. **Potential false positives**: sertraline, oxaprozin, & trazodone.
Buprenorphine	3-4 days	Negative on opiate screen. **Potential false positive**: tramadol.

Table abbreviations: BZ = benzoylecgonine; THC = Tetrahydrocannabinol

Urine Drug Testing Window of Detection Continued[33]

Drug	Detection Window	Comments
Cannabis	Infrequent: 1-3 days Chronic: <30 days	**False positives**: efavirenz, ibuprofen, naproxen, and pantoprazole.
Cocaine	2-4 days; 10-22 days if heavy chronic use	N/A
Codeine	1-2 days	**Positive test**: morphine, codeine, high-dose hydrocodone Positive on opiate immunoassay.
Fentanyl	1-2 days ***may vary widely***	Negative on opiate screen.
Heroin	1-4 days	**Positive test**: morphine, codeine. Positive on opiate immunoassay.
Hydrocodone	1-6 days	**Positive test**: hydrocodone, hydromorphone. Negative on opiate immunoassay.
Hydromorphone	1-2 days	**Positive test**: may not be detected. Negative on opiate immunoassay.
Methadone	2-11 days	Negative on opiate immunoassay. **Potential false positives**: chlorpromazine, diphenhydramine, quetiapine, verapamil
Morphine	1-4 days	**Positive test**: morphine, hydromorphone. Positive on opiate immunoassay.
Oxycodone	1-4 days	Typically negative on opiate immunoassay.
Phencyclidine (PCP)	1-30 days	**Potential false positives**: ibuprofen, dextromethorphan, venlafaxine

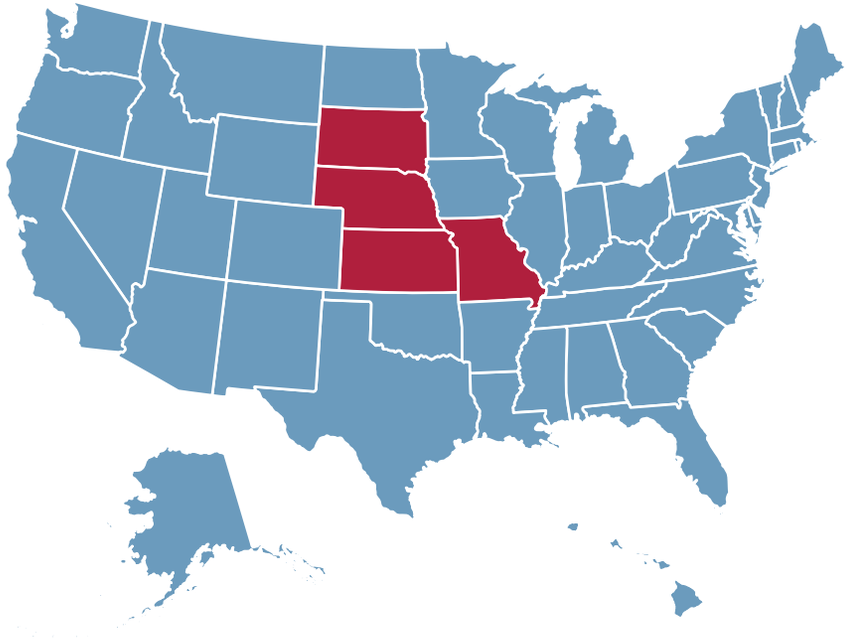
Note: ALL opiates may show false positives with quinolones.

PDMP (Prescription Drug Monitoring Program)

Before initiating treatment for OUD, providers should check their state's PDMP to determine whether their patient receives controlled substances from other healthcare providers.[33] Opioid treatment programs (OTPs) are not permitted to disclose methadone use to PDMPs, and some states do not report medical marijuana use to PDMPs. However, buprenorphine and other controlled substances are reported to PDMPs.[33]

States vary in who can access the PDMP. Pharmacists and providers typically have access; however, in many states, health service professionals, such as behavioral health professionals without prescribing authority, psychologists, and emergency medical services do not have access.[34] Regularly checking the PDMP can aid in screening, assessment, and ongoing treatment of patients with OUD and other substance use disorders.

States and Territories with Requirements for Providers to Check PDMP, as of December 2020[34]



= No requirement

Treatment of OUD

The treatment of OUD does not fit an acute care paradigm, with the objective of cure, but rather should be viewed as management of a lifelong, chronic condition with high rates of relapse. Long-term management objectives include:[35]

- Reduced risk of death and disease
- Improvement in mental & physical health and overall quality of life
- Restoration of social role impaired through unemployment, disrupted family relations, and involvement with the criminal justice system

When discussing treatment options, clinicians must be cognizant of the patient's willingness and motivation to be treated for OUD. Clinical guidelines support the use of medications for OUD (MOUD) for years, decades, and even a lifetime if patients are benefiting.[33] Even if the patient declines MOUD, reduction of harm and drug activity can make considerable impacts on health outcomes.

The objective of MOUD is to prevent withdrawal symptoms and cravings and allow the patient to function normally, attend school or work, and participate in other forms of treatment or recovery support services.[37] MOUD has been shown to improve mortality, treatment retention, and remission.[36] A recent comparative analysis of 40,885 individuals with OUD reported that use of methadone or buprenorphine resulted in a reduced risk of overdose during 3-month and 12-month follow-up by 76% and 59%, respectively.[36]

Buprenorphine/Methadone Initiation vs No Treatment[36]

Reduced inpatient detoxification & residential treatment episodes

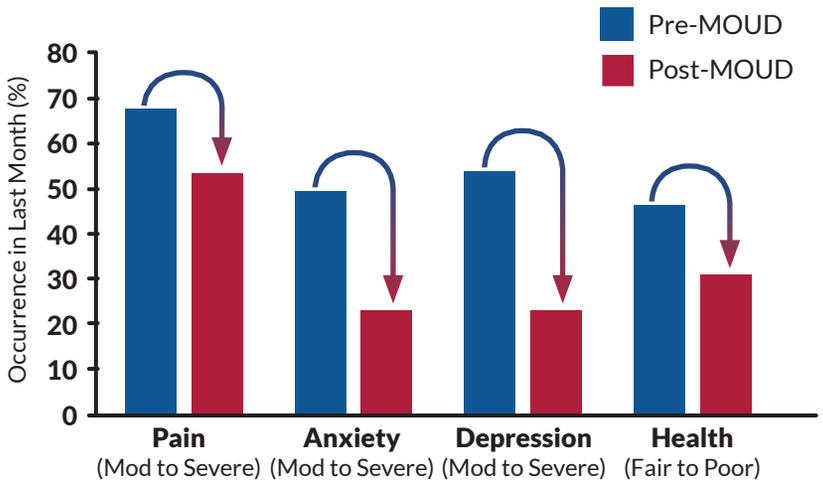
Reduced overdose rates by 76% at 3 months & 59% at 12 months

Reduced opioid-related ED visits & hospitalizations by 32% at 3 months & 26% at 12 months

Reduced total cost of care at 3 months & 12 months

Treatment of OUD

Physical and Mental Changes After MOUD Treatment[38]



"As rates of opioid-related death have increased despite decreases in prescription opioid supply, there is an increasing recognition that greater attention must be paid to improving access to effective OUD treatment."[36]

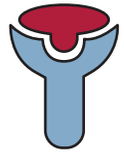
Despite the positive outcomes associated with MOUD, evidence indicates approximately 1 million people with OUD go untreated with MOUD annually.[39] Access to MOUD, along with behavioral health services, is an essential factor in the successful treatment of OUD, yet a 2020 study examined patient access to over 500 providers listed in the SAMHSA Buprenorphine Practitioner Locator and found only 28% of providers had appointments available.[40] In 2018, 40% of counties in the United States did not have any providers available who could prescribe buprenorphine for OUD.[41]

If not directly providing MOUD to the patient with OUD, clinicians must ensure that referrals to providers and treatment programs are successfully arranged in a timely manner and should follow up on the status of their patients' progress throughout the treatment process.

Medications for OUD Treatment

There are three medications currently available in the United States for the treatment of OUD: methadone, buprenorphine, and naltrexone.

Overview of MOUD[33]

	Methadone	Buprenorphine	Naltrexone
Mechanism of Action	 **Full agonist**	 **Partial agonist**	 **Antagonist**
Phase of Treatment	Medically supervised withdrawal, maintenance	Medically supervised withdrawal, maintenance	Prevention of relapse to opioid misuse, following medically supervised withdrawal
Route of Admin.	Oral	SL, buccal, implant, SC-ER	Oral, IM-ER
Possible Adverse Effects	Constipation, hyperhidrosis, respiratory depression, sedation, QT prolongation, sexual dysfunction, severe hypotension, misuse potential, NAS	Constipation, nausea, precipitated opioid withdrawal, excessive sweating, insomnia, pain, peripheral edema, respiratory depression, misuse potential, NAS	Nausea, anxiety, insomnia, precipitated opioid withdrawal, hepatotoxicity, vulnerability to opioid overdose, depression, suicidality, muscle cramps, dizziness or syncope, somnolence or sedation, appetite disorders Injection site reactions with IM-ER
Availability	**Schedule II** Only available at federally certified OTPs and the acute inpatient hospital setting.	**Schedule III** Requires waiver to prescribe. **Implant/SC:** requires REMS certification	**Not scheduled** Not included in OTP regulations Requires a prescription

ER = extended release; IM = intramuscular; NAS = neonatal abstinence syndrome; SC = subcutaneous; SL = sublingual

OUD Treatment Pathway

Individual with OUD

Essential Harm Reduction

- HBV vaccination
- Screening for HCV and HIV; if positive, initiate treatment
- Overdose risk awareness
- Overdose management training for self and family
- Take-home naloxone
- Education about safer injecting practices
- Needle and syringe exchange

Early/Mild OUD

Explain options

- prescribed detox
- home-based or in-patient options

Post-detox option of naltrexone (oral or depot)

If abstinence is not achieved, and especially if already dependent, consider MOUD

Consider NA or other mutual aid group

Consider residential rehab or drug-free therapeutic community

NA = Narcotics Anonymous

Source[2]

Established Moderate to Severe OUD

Encourage initiation onto OAT or other MOUD

- Variants: OAT (methadone, buprenorphine) or opioid antagonist/blocker therapy (naltrexone)
- Option of extended-release buprenorphine or naltrexone
- Assess for psychiatric comorbidities and, if present, treat

If MOUD not possible, not available, or if declined

Consider detox in

- Community/home
- Inpatient/ residential
- Consider option of naltrexone to protect against relapse and overdose

If OAT with failing or suboptimal benefit

- Correct/adjust MOUD dose or choice of specific MOUD
- Enhance support: psychological/social measures
- Consider facilitation of engagement with NA

If OAT still failing

Discuss options

- Therapeutic community
- Trial of more intense interventions

If OAT with good response

Addition of social and psychological support

Progressively reduced extent of supervision (e.g., take-home doses, less frequent appointments)

Further recovery support addressing family, employment, education, etc.

Essential harm reduction

- Overdose training
- Take-home naloxone
- Relapse management

Methadone

Methadone is the most used medication for OUD in the world, and the World Health Organization (WHO) considers it an essential medication. Numerous studies have shown methadone effectively reduces illicit opioid use, treats OUD, and retains patients in treatment better than placebo or no treatment. Only federally-certified OTPs may prescribe methadone for OUD, and there are over 1500 OTPs in the United States offering methadone.[33]

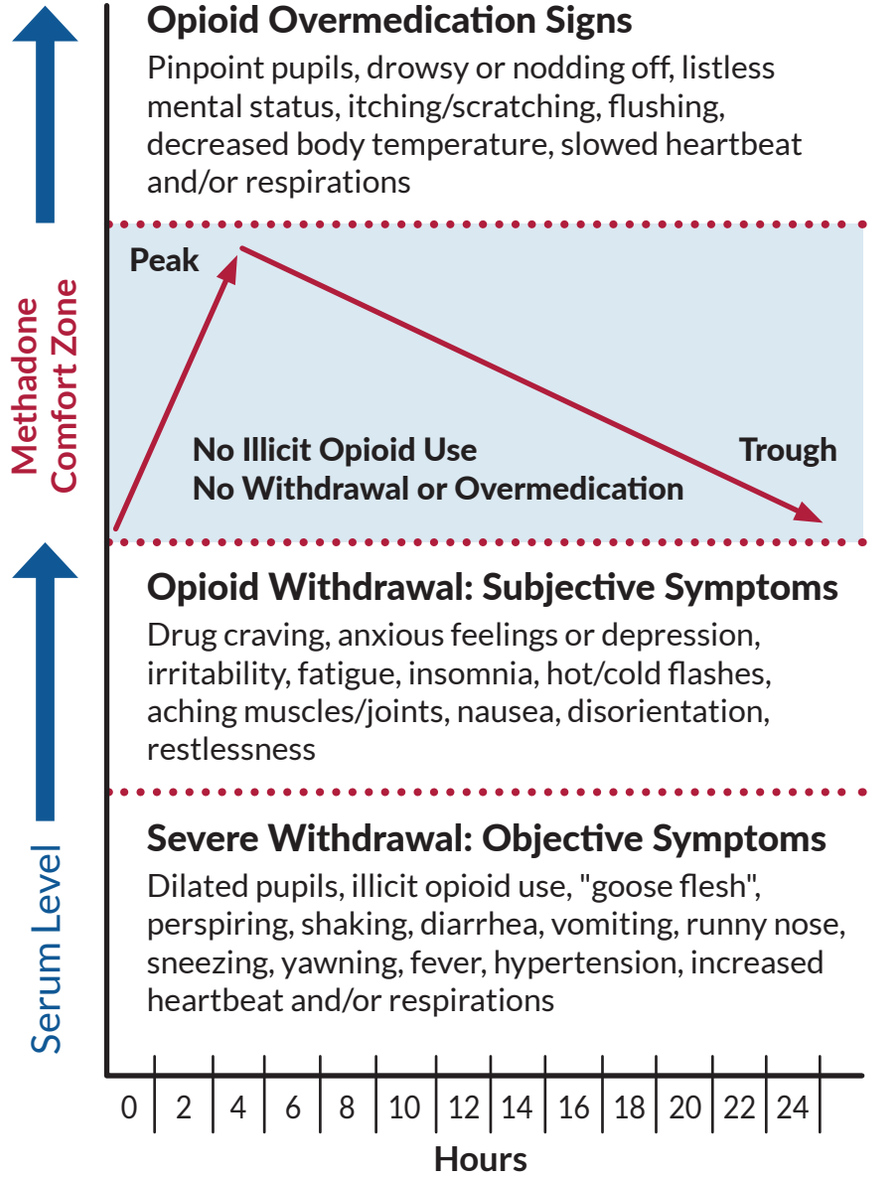
Methadone is a full μ-opioid receptor agonist and NMDA receptor antagonist administered in an oral liquid form.[42] Due to its prolonged half-life (~24 hours, although this can vary widely from 8-59 hours), methadone tends to accumulate with repeated dosing. Therefore, initiation of treatment begins with a low dose and escalates slowly.[2,33] Similarly, methadone must be discontinued via a slow taper spanning several weeks or months to avoid opioid withdrawal symptoms.[2,21]

Primarily metabolized by CYP3A4 (along with CYP2D6 and CYP1A2), methadone interacts with several medications.[42] Safety monitoring is essential, as drugs that inhibit methadone metabolism increase the risk of overdose (methadone has no ceiling effect) with similar mechanisms leading to respiratory depression and dangers as illicit opioid use.[33,42] Methadone also carries a risk of prolonged QT interval, so a baseline ECG, screening for cardiovascular comorbidities, and periodic monitoring are recommended.

Methadone has **no ceiling effect**.

"Although only OTPs can administer or dispense methadone for OUD, all healthcare professionals and addiction and mental health counselors should be familiar with methadone. Their patients may be enrolled in or need referral to OTPs." [33]

Using Signs & Symptoms to Determine Optimal Methadone Level[33]



Methadone

Methadone Highlights[33]

- Methadone reduces opioid craving and withdrawal and blunts or blocks the effects of illicit opioids.
- Methadone induction should begin at a low dose and increase gradually with daily monitoring over days or weeks.
  - This means that patients will not feel the full effect of the initial dose for 4 or more days
- Dosing must be individualized because methadone's bioavailability, clearance, and half-life can vary considerably among patients.
- Methadone has no ceiling effect.
- Methadone can cause respiratory depression, particularly during initial dosing and dose titration.
  - Concurrent misuse of alcohol or benzodiazepines with methadone (or buprenorphine) increases respiratory depression risk.
- Methadone has more clinically significant drug–drug interactions than buprenorphine. Adjustments to methadone dosing for drug-drug interactions should be coordinated with prescribing OTP.
  - Medications that induce CYP450 activity can increase methadone metabolism (i.e. dose would need to be increased to maintain benefits for recovery): some antibiotics, anticonvulsants, and antiretrovirals
  - Medications that inhibit CYP450 activity can decrease methadone metabolism (i.e. dose would need to be decreased to avoid negative side effects): some antibiotics, antacids, antifungals, antidepressants
- Duration of methadone treatment
  - Longer lengths of stay in methadone treatment are associated with superior treatment outcomes
- Patients should continue as long as they benefit, want to, and develop no contraindications

Buprenorphine

Buprenorphine is a partial μ-opioid receptor agonist as well as a κ-opioid receptor antagonist. It also has nociception receptor partial agonist properties. Buprenorphine is available in several formulations, including immediate-release sublingual and buccal formulations and extended-release injection and implant formulations.[33,43] In addition to monotherapy, buprenorphine is available in combination with naloxone, an opioid antagonist similar to naltrexone and designed to reverse overdose. The combination is intended to deter potential parenteral misuse through the precipitation of withdrawal symptoms upon injection;[2] naloxone is mostly inactive unless injected (very low bioavailability when taken sublingually).

Buprenorphine has demonstrated efficacy in retaining patients in treatment and reducing illicit opioid use compared to placebo or no medications. Like methadone, the WHO considers buprenorphine an essential medication.[33]

The partial agonist properties of buprenorphine create an opioid ceiling effect, meaning it is less likely than methadone to cause respiratory depression in accidental overdose. However, lethal overdose of buprenorphine is possible when given to opioid-naïve individuals or in combination with CNS depressants, such as benzodiazepines or alcohol.[33] Patients should be aware that starting buprenorphine may precipitate opioid withdrawal, particularly if other opioids, such as methadone or fentanyl, are still substantially occupying the μ-opioid receptor, as buprenorphine has weaker agonist effects but stronger receptor affinity allowing it to displace full agonists from receptors. For this reason, patients are typically advised to abstain from opioid use prior to beginning buprenorphine therapy. [2,33]

Buprenorphine **has a ceiling effect.**

Only providers with DEA-X waivers can prescribe buprenorphine for OUD.

Buprenorphine

- Must be in at least mild-to-moderate opioid withdrawal in order to begin induction
  - The more severe the withdrawal, the greater the relief
- Long-acting formulations (depot and implant) require clinical stabilization on transmucosal formulations prior to induction
- Withdrawal symptoms typically begin
  - 6-24 hours after last dose of a short-acting opioid like heroin
  - 24-96 hours after last dose of long acting opioids like methadone
  - Fentanyl half-life can be highly variable in terms of onset of withdrawal symptoms
- Induction is guided by use of the Clinical Opioid Withdrawal Scale (COWS)
  - COWS ≥8 or...
  - COWS <8 *and* no self-reported opioid use in the past 3 days *and* clinical UDS negative for opioids

The COWS[44]

For each item, circle the number that best describes the patient's signs or symptoms. Rate on just the apparent relationship to opioid withdrawal.

Sign/Symptom	Points
1. Resting Pulse Rate	
≤80	0
81-100	1
101-120	2
>120	4
2. Sweating	
No chills or flushing	0
Subjective chills/flushing	1
Flushed or observable moisture on face	2
Beads of sweat on brow/face	3
Sweat streaming off face	4
3. GI Upset	
No GI symptoms	0
Stomach cramps	1
Nausea or loose stool	2
Vomiting or diarrhea	3
Multiple episodes of diarrhea or vomiting	5
4. Tremor (hands)	
No tremor	0
Tremor felt but not observed	1
Slight tremor observable	2
Gross tremor or muscle twitching	4
5. Restlessness	
Able to sit still	0
Reports difficulty sitting still, but is able to do so	1
Frequent shifting or extraneous movements of arms/legs	3
Unable to sit still for more than a few seconds	5
6. Pupil Size	
Pupils pinpoint or normal	0
Pupils larger than normal	1
Pupils moderately dilated	2
Pupils so dilated that only the rim of the iris is visible	5
7. Bone or Joint Aches	
Not present	0
Mild discomfort	1
Severe diffuse ache	2
Unable to sit still because of discomfort	4
8. Runny Nose	
Not present	0
Nasal stuffiness/moist eyes	1
Nose running or tearing	2
Nose constantly running/ tears streaming down cheeks	4
9. Yawning	
No yawning	0
Yawning once/twice	1
Yawning 3+ times	2
Yawning several times per minute	4
10. Anxiety/Irritability	
None	0
Patient reports increasing irritability or anxiousness	1
Patient obviously irritable or anxious	2
Patient so irritable or anxious that participation in the assessment is difficult	4
11. Gooseflesh Skin	
Skin is smooth	0
Piloerection can be felt	3
Prominent piloerection	5

Max Possible Score: 48

Total Score

(sum of all 11 items)

5-12	Mild withdrawal
13-24	Moderate withdrawal
25-36	Moderate-severe withdrawal
>36	Severe withdrawal

Buprenorphine

Buprenorphine* Formulations & Dosing[33]

	Formulation/ Frequency	Dosages Available (mg)	Concomitant Naloxone?
Buprenorphine	SL tablets/daily	2 mg, 8 mg	No
Buprenorphine/ Naloxone	SL tablets/daily	2/0.5 mg, 8/2 mg	Yes
Suboxone® *(buprenorphine/ naloxone)*	SL film/daily	2/0.5 mg, 4/1 mg, 8/2 mg, 12/3 mg	Yes
Zubsolv® *(buprenorphine/ naloxone)*	SL tablets/daily	1.4/0.36 mg, 2.9/0.71 mg, 5.7/1.4 mg, 8.6/2.1 mg, 11.4/2.9 mg	Yes
Sublocade® *(buprenorphine/ naloxone)*	Long-acting subcutaneous injectable/monthly	100 mg/0.5 mL 300 mg/1.5 mL	No
Probuphine® *(buprenorphine)*	Implant/every 6 months	4 implants, 80 mg/implant	No

**The above FDA-approved formulations are indicated for MOUD; however, not all FDA-approved formulations of buprenorphine are indicated for MOUD.*

When to Increase Buprenorphine Dose[33]

- Are patients taking medication correctly and as scheduled?
  - If patients are taking doses correctly, a dose increase may be indicated, if certain conditions exist.
- Are patients taking other medications that may interfere with buprenorphine metabolism?
- Craving can be a conditioned response. It may not decrease with dose increases if patients spend time with people who use opioids in their presence.
- Dose increases typically occur in 2 mg to 4 mg increments.
  - It will take about 5 to 7 days to reach steady-state plasma concentrations after a dose increase.
- Offer psychosocial referrals to help decrease and manage cravings.
- Determine whether nonpharmacological problems are contributing to the need for increase.

When to Decrease Buprenorphine Dose[33]

- Decrease the dose when there is evidence of dose toxicity (i.e., sedation or, rarely, clearly linked clinically relevant increases in liver function tests).
- Hold the dose when there is acute alcohol or benzodiazepine intoxication.

Buprenorphine Prescribing

The Drug Addiction Treatment Act of 2000 (DATA 2000) changed the treatment of OUD by allowing the prescription of buprenorphine by physicians in outpatient settings.[45,46] Revisions under the Comprehensive Addiction & Recovery (CARA-2016) and the Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment (SUPPORT-2018) Acts further expanded the prescribing of buprenorphine in outpatient settings by physicians, advanced practice registered nurses (NPs, CNSs, CNMs, & CRNAs) & physician assistants (PAs) holding a DEA-X (aka DATA-2000) waiver. APRNs and PAs can apply to treat more than 30 patients if they complete a 24-hour waiver training course. ALL clinicians must apply through SAMHSA for the DEA to issue the waiver to prescribe BUP for OUD.

Buprenorphine Highlights[33]

- Be aware of potential CYP450 3A4 inducers, substrates, and inhibitors while monitoring for potential drug–drug interactions.
- Buprenorphine has fewer clinically relevant drug interactions than methadone.
- Respiratory depression and overdoses are uncommon in adults, but they do happen.
- Unintentional pediatric exposure can be life threatening or fatal.
- Buprenorphine can cause precipitated opioid withdrawal because it has weaker opioid agonist effects and stronger receptor affinity than full agonists.
- Buprenorphine's side effects may be less intense than those of full agonists.

Naltrexone

Naltrexone is indicated for the prevention of return to opioid dependence following medically supervised opioid withdrawal.[47] As an μ-opioid and κ-opioid receptor antagonist, naltrexone blocks the receptor and will precipitate withdrawal if any residual opioids are present.[33,47]

Although highly effective at opioid blockade, oral naltrexone is rarely used in clinical practice due to problems with initiation and adherence. Abstinence from opioid use for a minimum of 7-10 days is recommended prior to beginning oral naltrexone, and for many patients, this is highly challenging or impossible.[2,47] In addition, a systematic review of controlled studies found that the oral formulation of naltrexone offered no superiority over placebo in the management of OUD.[48]

In 2010, the FDA approved an expanded indication for an injectable extended-release formulation of naltrexone, XR-NTX, that has demonstrated superiority to placebo or no medication in reducing the risk of return to opioid use.[33] Both formulations are extensively metabolized by the liver and kidneys but without metabolism through the CYP450 enzyme system. This means drug-drug interactions are limited with the use of naltrexone. XR-NTX (a.k.a. long-acting naltrexone) delivers steady drug concentrations for about one month, and repeat administration causes no accumulation of naltrexone or its metabolites.[33]

Oral Naltrexone vs XR-NTX[33,49]

Oral Naltrexone

- **Dose:** 50mg daily
- **Patient must be fully opioid abstinent before starting treatment**
- While not typically used for maintenance, oral NTX can be started while awaiting XR-NTX initiation or referral to specialty care
- Consider prescribing oral NTX to those receiving XR-NTX to maintain OUD recovery if delays occur between injections.

XR-NTX

- **Dose:** 380mg IM monthly
- **Fast metabolizers:** administer every 21 days
- **Patient must be fully opioid abstinent before starting treatment**
  - Naloxone challenge
- Few drug-drug interactions
- Found **superior** to usual treatment in delaying time to relapse

Naloxone Challenge Prior to XR-NTX Administration[33]

The naloxone challenge may be used to assess lack of physical dependence on opioids; however, a negative naloxone challenge does not guarantee that the patient will not experience precipitated opioid withdrawal upon naltrexone administration.[33]

Intravenous Administration

1. Draw 0.8 mg naloxone into a sterile syringe.
2. Inject 0.2 mg naloxone intravenously.
3. Wait 30 seconds for signs and symptoms of withdrawal. **If withdrawal signs/symptoms are present, stop the naloxone challenge and treat symptomatically**.
4. If no withdrawal signs and symptoms are present and vital signs are stable, inject remaining naloxone (0.6 mg) and observe for 20 minutes. **Check the patient's vital signs and monitor for withdrawal.**
5. If withdrawal signs and symptoms are present, stop the naloxone challenge and treat symptomatically. **The test can be repeated in 24 hours** or the patient can be considered for opioid agonist treatment.
6. If no withdrawal signs and symptoms are present and XR-NTX is the desired treatment course, administer XR-NTX in the upper outer quadrant of the buttock, following package insert directions.
7. **Instruct the patient about the risk of overdose and death if they use opioids to override the blockade.**

Subcutaneous Administration

1. Inject 0.8 mg naloxone subcutaneously.
2. Wait 20 minutes while checking vital signs and observing for signs and symptoms of opioid withdrawal.
3. **If withdrawal signs and symptoms are present, stop the naloxone challenge and treat symptomatically.** The test can be repeated within 24 hours, or the patient can be considered for opioid agonist treatment.
4. If no withdrawal signs and symptoms are present, follow Step 6 for XR-NTX treatment above.

Naltrexone

Naltrexone Highlights[33]

- Unlike methadone and buprenorphine, naltrexone will not alleviate withdrawal symptoms; however, if stopped, naltrexone will not cause withdrawal symptoms. In addition, naltrexone cannot be diverted.
- Oral naltrexone is not superior to placebo or to no medication in treatment retention or illicit opioid use reduction
- XR-NTX is more effective than placebo or no medication in reducing the risk of return to opioid use.
- Naltrexone has limited potential drug-drug interactions
- Pregnant women are not candidates for naltrexone therapy
- Precipitated opioid withdrawal can be severe enough to require hospitalization
  - Patient **MUST be free of ALL opioids and metabolites for a minimum of 7-10 days** prior to administration of naltrexone to avoid precipitated withdrawal
- Patients are vulnerable to opioid overdose death after completion of the dosing period
- Patient monitoring and education is essential
  - Hypersensitivity reactions, injection site reactions, depression/suicidal ideation, renal impairment, hepatitis
- Patients should carry written information with them at all times to alert healthcare providers that they are taking XR-NTX
  - May not respond to therapeutic effects of opioid-containing medicines for pain, cough, cold, or diarrhea

"Given the often-chronic nature of OUD and the potentially fatal consequences of unintended opioid overdose, it is critical that you base patients' length of time in treatment on their individual needs." [33]

Withdrawal Management

When beginning treatment for OUD, it is critical that clinicians recognize the impact of withdrawal symptoms on the patient and understand that the long term goal of therapy is not discontinuing MOUD but maintaining long-term recovery. Depending on the patient, MOUD may be necessary for weeks, months, years, or lifelong. Opioid tolerance typically prevents individuals with OUD from experiencing the euphoric effects of therapeutic doses of methadone and buprenorphine felt by those without OUD. Waned tolerance is why many patients overdose when returning to opioid use after prolonged abstinence.[37] Tapering MOUD should be a shared decision-making discussion with the patient and conducted very slowly to avoid relapse.[37]

*"**Severe opioid withdrawal isn't something I'd wish on my worst enemy.** The last time I went cold turkey, I was determined to come off all the way. The physical symptoms were just the tip of the iceberg. My mind was a nightmare that I thought I would never wake up from.*

***There were times when I was almost convinced that dying would be better than what I was feeling.** I did not experience a moment of ease for the first 3 months, and it was 6 months until I started to feel normal."* [33]

Withdrawal Symptom Management

Drug	Tablet Dose (q6 hours)	Indication
Clonidine HCl	0.1 mg	For severe headache, elevated blood pressure, & racing heart
Dicyclomine	20 mg	For abdominal cramping
Hydroxyzine HCl	50-100 mg	For anxiety & insomnia
Ibuprofen	600 mg	For body and joint aches and pain
Ondansetron HCl	4 mg	For nausea & vomiting

MOUD Comparison

Category	Methadone	Buprenorphine	Naltrexone
Typically for Patients with OUD who are...	Physiologically dependent on opioids and meet federal criteria for OTP admission	Physiologically dependent on opioids	Abstinent from short-acting opioids **for a minimum** of 7 days and long-acting opioids for 10-14 days
Misuse/ Diversion Potential	Low in OTPs with directly observed therapy. Moderate for take home doses.	Low in OTPs or other settings with observed dose administration. Moderate-high for take-home doses.	None
Retention in Treatment	Higher than no MOUD & placebo	Higher than no MOUD & placebo	**Oral:** no better than placebo or no MOUD **XR-NTX:** higher than no MOUD & placebo
Suppression of Illicit Opioid Use	**All are effective**		
Overdose Mortality	Lower	Lower	Unknown
Location/ Frequency of Office Visits	**OTP only:** 6-7 days/week initially; take-homes are allowed based on time in treatment & patient progress	**Office/clinic:** begins daily to weekly, then tailored to patient's needs **OTP:** can treat 6-7 days/week initially; take-homes allowed without the time-in-treatment requirements of methadone	**Office/clinic:** varies from weekly to monthly
Administration	Oral	Sublingual/buccal; SC injection; implant by specially trained provider, & **only for stabilized patients**	Oral or IM
Sedation	Low unless dose titration is too quick or dose is not adjusted for presence of concurrent substances	Low unless concurrent substances are present (e.g. alcohol, benzos)	None
Risk of Medication-Induced Respiratory Depression	Rare, although higher than buprenorphine. May be elevated in first 2 weeks.	Very rare. Lower than methadone.	None
Risk of Precipitated Withdrawal on Initiation	Can occur given unknown potency & half-life of fentanyl if in patient's system	Can occur if started too prematurely after recent opioid use	Can occur if any opioids remain in patient's system
Withdrawal Symptoms on Stopping	Present; higher than buprenorphine if abruptly discontinued	Present; lower than methadone if abruptly discontinued	None

Source[33]

"If a patient does not discontinue all illicit drugs for extended periods, it doesn't mean treatment has failed...It means the treatment plan may require modification to meet the patient's needs." [33]

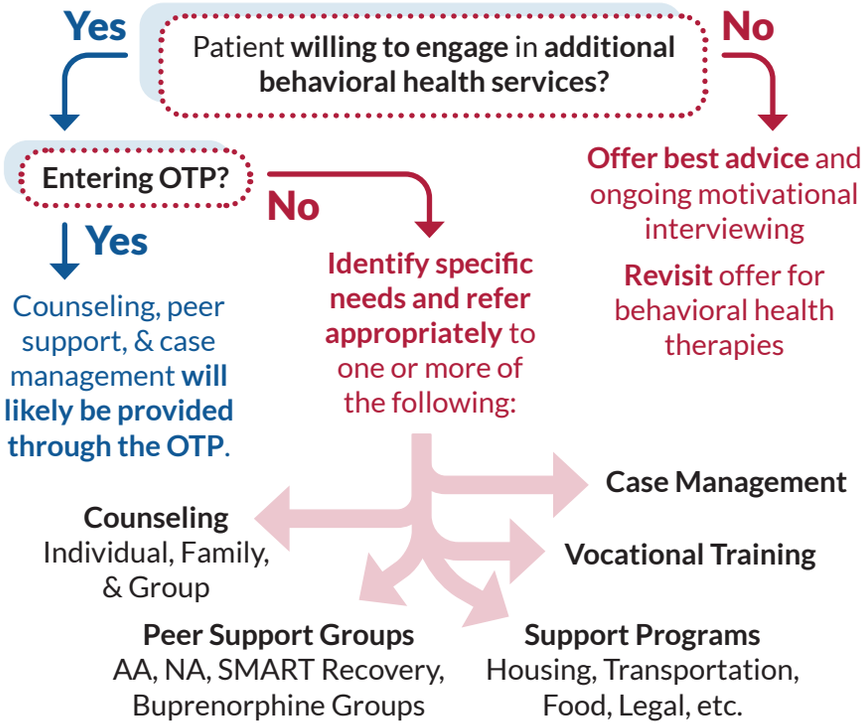
This is the premise of the harm reduction model.

Role of Behavioral Health

Addressing mental health needs is a critical and necessary component of addiction recovery and often overlooked. According to an analysis of the 2015-2018 National Survey of Drug Use and Health, the rate of suicidal behavior is significantly higher among those with OUD compared to those without OUD (22% vs 4%).[50]

Data indicate behavioral health services are not implemented effectively into clinical practice. A recent study analyzing the 2017 National Survey of Drug Use and Health found that 91.7% (almost 92%) do not receive treatment for co-morbid psychiatric & substance use disorders.[51] Another study found that financial difficulties accessing behavioral health services were a significant barrier for this population.[52]

Referring Patients Who Receive MOUD to Behavioral Health & Other Services[33]



Collaborative Care Model

Clinicians are encouraged by SAMHSA to coordinate primary care, behavioral health, and wraparound services needed and desired by patients to address their medical, social, and recovery needs.[33] In addition to behavioral health, caseworkers can help patients with housing support, insurance, income support, food assistance services, vocational and educational services, and counseling.[33]

The "Hub and Spoke" system is one solution to provide collaborative care, and in 2013, the Centers for Medicare & Medicaid Services granted Vermont a Health Home State Plan amendment to transform existing MAT services into Hubs and Spokes. In 2019, the model was recognized by the Medicaid Innovation Accelerator Program.[53]

In this model, a Hub is a specialty treatment center responsible for the coordinating of care, including:[54]

- Provide comprehensive assessments and treatment protocols.
- Provide methadone treatment and supports.
- For clinically complex clients, initiate buprenorphine treatment and provide care for initial stabilization period.
- Coordinate referral to ongoing care.
- Provide specialty addictions consultation and support to ongoing care.
- Provide ongoing coordination of care for clinically complex clients

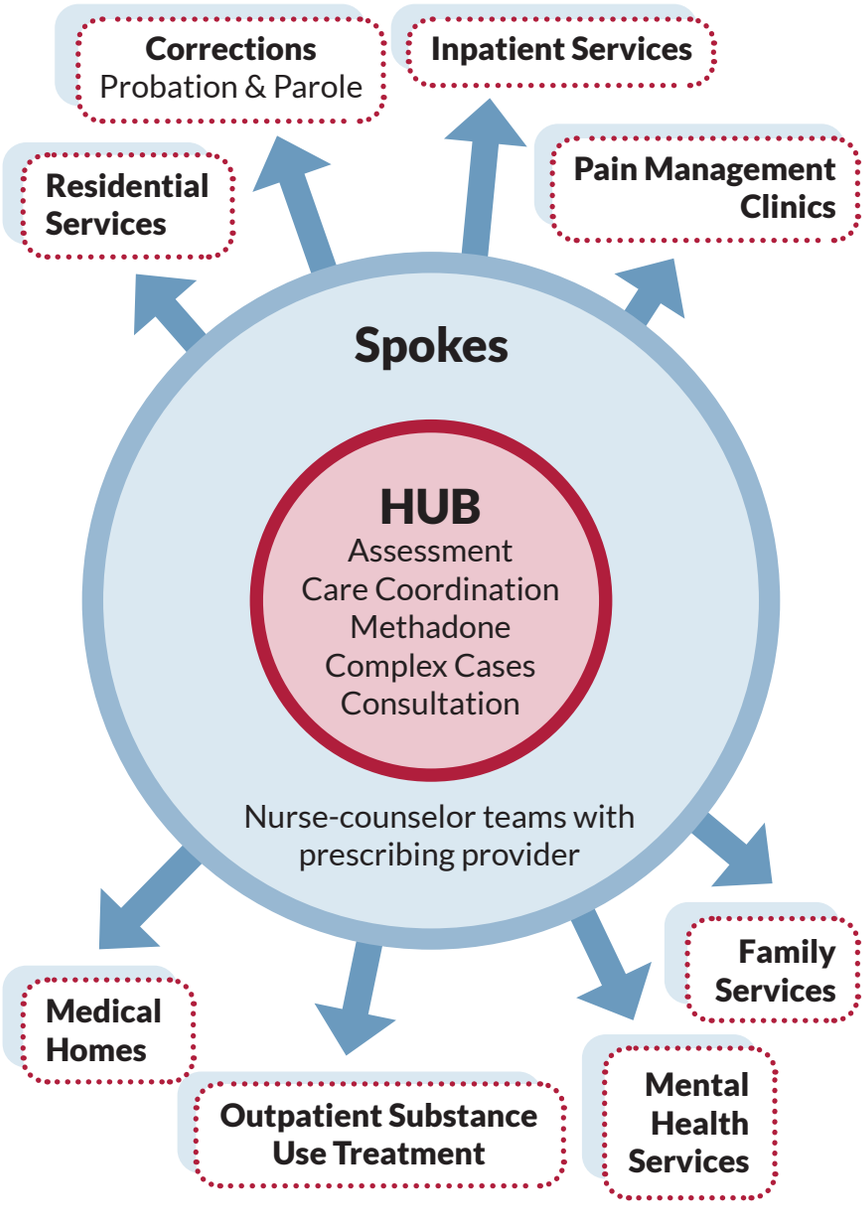
A Spoke is the ongoing care system comprised of a prescriber and collaborating health and addiction professionals who monitor treatment.[54]

See the next page for a diagram of the Hub and Spoke system.

> ***"Recovery status is best defined by factors other than medication status. N****either medication-assisted treatment of opioid [use disorder] nor the cessation of such treatment by itself constitutes recovery.* ***Recovery status instead hinges on broader achievements in health and social functioning—with or without medication support."*** [33]

Collaborative Care Model

Hub & Spoke System[54]



Resources

Opioid-Related Overdose Prevention

- Prescribe To Prevent: Provides information about naloxone prescribing for overdose prevention, including educational patient handouts and videos.
  http://prescribetoprevent.org
- SAMHSA Opioid Overdose Prevention Toolkit:
  https://store.samhsa.gov/product/Opioid-Overdose-Prevention-Toolkit/SMA18-4742
- CDC—Overdose Prevention: Provides links and tools for clinicians to help prevent opioid overdose deaths.
  www.cdc.gov/drugoverdose/prevention/index.html
- NIDA, Opioid Overdose Reversal with Naloxone (Narcan, Evzio):
  www.drugabuse.gov/related-topics/opioid-overdose-reversal-naloxone-narcan-evzio

Opioid Withdrawal Scales

- WHO Guidelines for the Psychosocially Assisted Pharmacological Treatment of Opioid Dependence: Annex 10: Provides COWS and other opioid withdrawal scales.
  www.ncbi.nlm.nih.gov/books/NBK143183
- The Clinical Institute Narcotic Assessment Scale for Withdrawal Symptoms
  https://ncpoep.org/wp-content/uploads/2015/02/Appendix_7_Clinical_Institute_Narcotic_Assessment_CINA_Scale_for_Withdrawal_Symptoms.pdf

Syringe Exchange

- North American Syringe Exchange Network: Provides a national directory of syringe exchange programs in the United States.
  https://nasen.org/directory

Resources Continued

Treatment Locators

- Buprenorphine Treatment Practitioner Locator
  www.samhsa.gov/medication-assisted-treatment/physician-program-data/treatment-physician-locator
- Behavioral Health Treatment Services Locator
  https://findtreatment.samhsa.gov/
- Opioid Treatment Program Directory
  https://dpt2.samhsa.gov/treatment/directory.aspx

Buprenorphine Training, Mentorship, and Waivers

- SAMHSA, Buprenorphine Waiver Management
  www.samhsa.gov/medication-assisted-treatment/training-materials-resources/apply-for-practitioner-waiver
- SAMHSA, Buprenorphine Practice Guidelines
  www.federalregister.gov/documents/2021/04/28/2021-08961/practice-guidelines-for-the-administration-of-buprenorphine-for-treating-opioid-use-disorder
- SAMHSA, Qualify for a Practitioner Waiver
  www.samhsa.gov/medication-assisted-treatment/training-materials-resources/apply-for-practitioner-waiver
- PCSS-MAT: Provides buprenorphine waiver training and mentorship for healthcare professionals. Includes updates and other resources about MOUD.
  https://pcssnow.org/

Helplines

- For information on buprenorphine waiver, contact the SAMHSA Center for Substance Abuse Treatment (CSAT) at 866-BUP-CSAT (866-287-2728) or infobuprenorphine@samhsa.hhs.gov
- Patient Hotlines
  - **SAMHSA's National Helpline: 1-800-662-HELP (4357)**
  - **Suicide Prevention Lifeline: 1-800-273-TALK (8255)**

Conclusion

The burden of OUD on patients, families, the healthcare system, and communities is substantial, and increasingly unacceptable numbers of individuals with OUD go untreated and/or die each year. Given that OUD is a chronic and relapsing disease, healthcare providers need to prepare for the relapses and remissions of the recovery process. Adopting the chronic care model of prevention, early intervention, treatment, and support for recovery will allow us to partner with our patients early in the disease process. As advanced practice nurses, we must be prepared to screen patients for OUD with the compassion, empathy, and understanding that is ubiquitous to nursing. Engaging the techniques of motivational interviewing, we can assess out patient's readiness and provide education, intervention, treatment and/or referral for specialty care.

Understanding that OUD is a disease that incorporates biological, environmental and psychosocial factors, a diagnosis of OUD is the first step in the recovery journey. MOUD serves as the foundation for the biological and physical recovery. Three medications are available for MOUD: methadone, buprenorphine, and naltrexone; selecting the course of therapy should be individualized to each patient and involve shared decision-making and patient education. Examining the patient's environment and readiness to engage in treatment encompasses the psychosocial aspects of recovery. In patients who are not ready for MOUD, clinicians should implement harm reduction strategies and offer referral to behavioral health services. The management of OUD requires a collaborative care approach, by enlisting various healthcare professionals across disciplines and settings.

Although OUD is a chronic, relapsing disorder, we as nurses are privileged to guide our patients in their healing and recovery. Through the use of MOUD and psychosocial interventions, our patients can reintegrate into society, their families and the workforce; they can improve their physical and mental health; and they can achieve their optimal quality of life.

"Before the uniqueness of each situation, indeed, it is never enough to follow a protocol, but a constant (and tiresome) effort of discernment and attention to the individual person is required. All this makes your profession [nursing] a veritable mission and make you [nurses] experts in humanity."
– Pope Francis

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"When you are a nurse, you know that everyday you will touch a life or a life will touch yours."
–NHS Wales

"To do what nobody else will do, in a way that nobody else can do, in spite of all we go through, that is what it is to be a nurse."
–Rawsi Williams

"I'm an ex-convict. I have AIDS. I'm a prostitute. I'm poor. I'm old. I'm a lesbian. I aborted my baby. I'm a teenage mom. I'm a victim of rape. I'm a drug addict. I'm alcoholic. I'm a beggar. I have cancer. I have a contagious disease….but the nurse said, I'll Take Care of You."
–Unknown

"Too often we underestimate the power of a touch, a smile, a kind word, a listening ear, an honest accomplishment, or the smallest act of caring, all of which have the potential to turn a life around."
–Leo Buscalgia

"The opposite of addiction is not sobriety, but human connection."
–Johann Hari

"There are multiple pathways of addiction recovery and all are a cause of celebration."
–William L White