Substance Abuse

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Treatment Approaches for Drug Addiction

Note: Chapters 1 – 4 are from the National Institute on Drug Abuse (NIH); National Institutes of Health; U.S. Department of Health and Human Services. Updated January 2019

Chapter 1 – Introduction

What is drug addiction?
Drug addiction is a chronic disease characterized by compulsive, or uncontrollable, drug seeking and use despite harmful consequences and changes in the brain, which can be long lasting. These changes in the brain can lead to the harmful behaviors seen in people who use drugs. Drug addiction is also a relapsing disease. Relapse is the return to drug use after an attempt to stop.

The path to drug addiction begins with the voluntary act of taking drugs. But over time, a person's ability to choose not to do so becomes compromised. Seeking and taking the drug becomes compulsive. This is mostly due to the effects of long-term drug exposure on brain function. Addiction affects parts of the brain involved in reward and motivation, learning and memory, and control over behavior.

Addiction is a disease that affects both the brain and behavior.

Can drug addiction be treated?
Yes, but it's not simple. Because addiction is a chronic disease, people can't simply stop using drugs for a few days and be cured. Most patients need long-term or repeated care to stop using completely and recover their lives.

Addiction treatment must help the person do the following:

- stop using drugs
- stay drug-free

- be productive in the family, at work, and in society

B. Principles of Effective Treatment

Based on scientific research since the mid-1970s, the following key principles should form the basis of any effective treatment program:

- Addiction is a complex but treatable disease that affects brain function and behavior.
- No single treatment is right for everyone.
- People need to have quick access to treatment.
- Effective treatment addresses all of the patient's needs, not just his or her drug use.
- Staying in treatment long enough is critical.
- Counseling and other behavioral therapies are the most commonly used forms of treatment.
- Medications are often an important part of treatment, especially when combined with behavioral therapies.
- Treatment plans must be reviewed often and modified to fit the patient's changing needs.
- Treatment should address other possible mental disorders.
- Medically assisted detoxification is only the first stage of treatment.
- Treatment doesn't need to be voluntary to be effective.
- Drug use during treatment must be monitored continuously.
- Treatment programs should test patients for HIV/AIDS, hepatitis B and C, tuberculosis, and other infectious diseases as well as teach them about steps they can take to reduce their risk of these illnesses.

What are treatments for drug addiction?

There are many options that have been successful in treating drug addiction, including:

- behavioral counseling
- medication
- medical devices and applications used to treat withdrawal symptoms or deliver skills training
- evaluation and treatment for co-occurring mental health issues such as depression and anxiety
- long-term follow-up to prevent relapse

A range of care with a tailored treatment program and follow-up options can be crucial to success. Treatment should include both medical and mental health services as needed.
Follow-up care may include community- or family-based recovery support systems.

C. How are medications used in drug addiction treatment?

Medications can be used to manage withdrawal symptoms, prevent relapse, and treat co- occurring conditions.

Withdrawal. Medications help suppress withdrawal symptoms during detoxification. Detoxification is not in itself "treatment," but only the first step in the process. Patients who do not receive any further treatment after detoxification usually resume their drug use. One study of treatment facilities found that medications were used in almost 80 percent of detoxifications (SAMHSA, 2014). Devices are also being used to reduce withdrawal symptoms. In November 2017, the Food and Drug Administration (FDA) granted a new indication to an electronic stimulation device, NSS-2 Bridge, for use in helping reduce opioid withdrawal symptoms. This device is placed behind the ear and sends electrical pulses to stimulate certain brain nerves.

Relapse prevention. Patients can use medications to help re-establish normal brain function and decrease cravings. Medications are available for treatment of opioid (heroin, prescription pain relievers), tobacco (nicotine), and alcohol addiction. Scientists are developing other medications to treat stimulant (cocaine, methamphetamine) and cannabis (marijuana) addiction. People who use more than one drug, which is very common, need treatment for all of the substances they use.

- ***Opioids:*** Methadone (Dolophine®, Methadose®), buprenorphine (Suboxone®, Subutex®, Probuphine® , Sublocade™), and naltrexone (Vivitrol®) are used to treat opioid addiction. Acting on the same targets in the brain as heroin and morphine, methadone and buprenorphine suppress withdrawal symptoms and relieve cravings. Naltrexone blocks the effects of opioids at their receptor sites in the brain and should be used only in patients who have already been detoxified. All medications help patients reduce drug seeking and related criminal behavior and help them become more open to behavioral treatments. A NIDA study found that once treatment is initiated, both a buprenorphine/naloxone combination and an

extended release naltrexone formulation are similarly effective in treating opioid addiction. Because full detoxification is necessary for treatment with naloxone, initiating treatment among active users was difficult, but once detoxification was complete, both medications had similar effectiveness.□

- ***Tobacco:*** Nicotine replacement therapies have several forms, including the patch, spray, gum, and lozenges. These products are available over the counter. The U.S. Food and Drug Administration (FDA) has approved two prescription medications for nicotine addiction: bupropion (Zyban®) and varenicline (Chantix®). They work differently in the brain, but both help prevent relapse in people trying to quit. The medications are more effective when combined with behavioral treatments, such as group and individual therapy as well as telephone quit-lines.
    - ***Alcohol:*** Three medications have been FDA-approved for treating alcohol addiction and a fourth, topiramate, has shown promise in clinical trials (large- scale studies with people). The three approved medications are as follows **Naltrexone** blocks opioid receptors that are involved in the rewarding effects of drinking and in the craving for alcohol. It reduces relapse to heavy drinking and is highly effective in some patients. Genetic differences may affect how well the drug works in certain patients.
    - **Acamprosate (Campral®)** may reduce symptoms of long-lasting withdrawal, such as insomnia, anxiety, restlessness, and dysphoria (generally feeling unwell or unhappy). It may be more effective in patients with severe addiction.
    - **Disulfiram (Antabuse®)** interferes with the breakdown of alcohol. Acetaldehyde builds up in the body, leading to unpleasant reactions that include flushing (warmth and redness in the face), nausea, and irregular heartbeat if the patient drinks alcohol. Compliance (taking the drug as prescribed) can be a problem, but it may help patients who are highly motivated to quit drinking.

- ***Co-occuring conditions:*** Other medications are available to treat possible mental health conditions, such as depression or anxiety, that may be contributing to the person's addiction.

D. How are behavioral therapies used to treat drug addiction?

Behavioral therapies help patients:

- modify their attitudes and behaviors related to drug use
- increase healthy life skills

- persist with other forms of treatment, such as medication

Patients can receive treatment in many different settings with various approaches.

Outpatient behavioral treatment includes a wide variety of programs for patients who visit a behavioral health counselor on a regular schedule. Most of the programs involve individual or group drug counseling, or both. These programs typically offer forms of behavioral therapy such as:

- *cognitive-behavioral therapy,* which helps patients recognize, avoid, and cope with the situations in which they are most likely to use drugs
- *multidimensional family therapy*—developed for adolescents with drug abuse problems as well as their families—which addresses a range of influences on their drug abuse patterns and is designed to improve overall family functioning
- *motivational interviewing,* which makes the most of people's readiness to change their behavior and enter treatment
- *motivational incentives* (contingency management), which uses positive reinforcement to encourage abstinence from drugs

Treatment is sometimes intensive at first, where patients attend multiple outpatient sessions each week. After completing intensive treatment, patients transition to regular outpatient treatment, which meets less often and for fewer hours per week to help sustain their recovery. In September 2017, the FDA permitted marketing of the first mobile application, reSET®, to help treat substance use disorders. This application is intended to be used with outpatient treatment to treat alcohol, cocaine, marijuana, and stimulant substance use disorders. In December 2018, the FDA cleared a mobile medical application, reSET®, to help treat opioid use disorders. This application is a prescription cognitive behavioral therapy and should be used in conjunction with treatment that includes buprenorphine and contingency management.

Inpatient or residential treatment can also be very effective, especially for those with more severe problems (including co-occurring disorders). Licensed residential treatment facilities offer 24-hour structured and intensive care, including safe housing and medical attention. Residential treatment facilities may use a variety of therapeutic approaches, and they are generally aimed at helping

the patient live a drug-free, crime-free lifestyle after treatment. Examples of residential treatment settings include:

- *Therapeutic communities*, which are highly structured programs in which patients remain at a residence, typically for 6 to 12 months. The entire community, including treatment staff and those in recovery, act as key agents of change, influencing the patient's attitudes, understanding, and behaviors associated with drug use. Read more about therapeutic communities in the *Therapeutic Communities Research Report* at https://www.drugabuse.gov/publications/ research-reports/therapeutic-communities.
- *Shorter-term residential treatment*, which typically focuses on detoxification as well as providing initial intensive counseling and preparation for treatment in a community-based setting.
- *Recovery housing,* which provides supervised, short-term housing for patients, often following other types of inpatient or residential treatment. Recovery housing can help people make the transition to an independent life—for example, helping them learn how to manage finances or seek employment, as well as connecting them to support services in the community.

Challenges of Re-entry

Drug abuse changes the function of the brain, and many things can "trigger" drug cravings within the brain. It's critical for those in treatment, especially those treated at an inpatient facility or prison, to learn how to recognize, avoid, and cope with triggers they are likely to be exposed to after treatment.

E. Is treatment different for criminal justice populations?

Scientific research since the mid-1970s shows that drug abuse treatment can help many drug-using offenders change their attitudes, beliefs, and behaviors towards drug abuse; avoid relapse; and successfully remove themselves from a life of substance abuse and crime. Many of the principles of treating drug addiction are similar for people within the criminal justice system as for those in the general population. However, many offenders don't have access to the types of services they need. Treatment that is of poor quality or is not well suited to the needs of offenders may not be effective at reducing drug use and criminal behavior.

In addition to the general principles of treatment, some considerations specific to offenders include the following:

- Treatment should include development of specific cognitive skills to help the offender adjust attitudes and beliefs that lead to drug abuse and crime, such as feeling entitled to have things one's own way or not understanding the consequences of one's behavior. This includes skills related to thinking, understanding, learning, and remembering.
- Treatment planning should include tailored services within the correctional facility as well as transition to community-based treatment after release.
- Ongoing coordination between treatment providers and courts or parole and probation officers is important in addressing the complex needs of offenders re- entering society.

How many people get treatment for drug addiction?

According to SAMHSA's National Survey on Drug Use and Health, 22.5 million people (8.5 percent of the U.S. population) aged 12 or older needed treatment for an illicit* drug or alcohol use problem in 2014. Only 4.2 million (18.5 percent of those who needed treatment) received any substance use treatment in the same year. Of these, about 2.6 million people received treatment at specialty treatment programs (CBHSQ, 2015).

*The term "illicit" refers to the use of illegal drugs, including marijuana according to federal law, and misuse of prescription medications.

F. Points to Remember

- Drug addiction can be treated, but it's not simple. Addiction treatment must help the person do the following:
  - stop using drugs
  - stay drug-free
  - be productive in the family, at work, and in society

- Successful treatment has several steps:
  - detoxification
  - behavioral counseling
  - medication (for opioid, tobacco, or alcohol addiction)
  - evaluation and treatment for co-occurring mental health issues such as depression and anxiety
  - long-term follow-up to prevent relapse

- Medications and devices can be used to manage withdrawal symptoms, prevent relapse, and treat co-occurring conditions.

- Behavioral therapies help patients:
  - modify their attitudes and behaviors related to drug use
  - increase healthy life skills
  - persist with other forms of treatment, such as medication

- People within the criminal justice system may need additional treatment services to treat drug use disorders effectively. However, many offenders don't have access to the types of services they need.

Learn More

For more information about drug addiction treatment, visit: www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based- guide-third-edition/acknowledgments

For information about drug addiction treatment in the criminal justice system, visit: www.drugabuse.gov/publications/principles-drug-abuse-treatment-criminal-justice- populations/principles

For step-by-step guides for people who think they or a loved one may need treatment, visit: www.drugabuse.gov/related-topics/treatment

References

Center for Behavioral Health Statistics and Quality (CBSHQ). *2014 National Survey on Drug Use and Health: Detailed Tables.* Rockville, MD: Substance Abuse and Mental Health Services Administration; 2015.

Substance Abuse and Mental Health Services Administration (SAMHSA). *National Survey of Substance Abuse Treatment Services (N-SSATS): 2013. Data on Substance Abuse Treatment Facilities.* Rockville, MD: Substance Abuse and Mental Health Services Administration; 2014. HHS Publication No. (SMA) 14-489. BHSIS Series S-73.

Chapter 2 – Health Effects of Specific Drugs

A. Anabolic Steroids

What are anabolic steroids?

Anabolic steroids are synthetic, or human-made, variations of the male sex hormone testosterone. The proper term for these compounds is *anabolic-androgenic steroids*. "Anabolic" refers to muscle building, and "androgenic" refers to increased male sex characteristics. Some common names for anabolic steroids are Gear, Juice, Roids, and Stackers.

Health care providers can prescribe steroids to treat hormonal issues, such as delayed puberty. Steroids can also treat diseases that cause muscle loss, such as cancer and AIDS. But some athletes and bodybuilders misuse these drugs in an attempt to boost performance or improve their physical appearance.

The majority of people who misuse steroids are male weightlifters in their 20s or 30s. Anabolic steroid misuse is much less common in women. It is difficult to measure steroid misuse in the United States because many national surveys do not measure it. However, use among teens is generally minimal. The 2016 NIDA-funded Monitoring the Future study has shown that past-year misuse of steroids has declined among 8th and 10th graders in recent years, while holding steady for 12th graders.

How do people misuse anabolic steroids?

People who misuse anabolic steroids usually take them orally, inject them into muscles, or apply them to the skin as a gel or cream. These doses may be 10 to 100 times higher than doses prescribed to treat medical conditions.

Commons patterns for misusing steroids include:

- cycling—taking multiple doses for a period of time, stopping for a time, and then restarting
- stacking—combining two or more different steroids and mixing oral and/or injectable types
- pyramiding—slowly increasing the dose or frequency of steroid misuse, reaching a peak amount, and then gradually tapering off to zero
- plateauing—alternating, overlapping, or substituting with another steroid to avoid developing a tolerance

There is no scientific evidence that any of these practices reduce the harmful medical consequences of these drugs.

How do anabolic steroids affect the brain?
Anabolic steroids work differently from other drugs of abuse; they do not have the same short-term effects on the brain. The most important difference is that steroids do not directly activate the reward system to cause a "high"; they also do not trigger rapid increases in the brain chemical dopamine, which reinforces most other types of drug taking behavior.

Misuse of anabolic steroids might lead to negative mental effects, such as:

- paranoid (extreme, unreasonable) jealousy
- extreme irritability and aggression ("roid rage")
- *delusions*—false beliefs or ideas
- impaired judgment
- mania

Anabolic Steroids and Infectious Diseases
People who inject steroids increase their risk of contracting or transmitting HIV/AIDS or hepatitis. Read more about this connection by visiting:

DrugFacts: Drug Use and Viral Infections
https://www.drugabuse.gov/publications/drugfacts/drug-use-viral-infections-hiv-hepatitis

Viral Hepatitis—A Very Real Consequence of Substance Use
https://www.drugabuse.gov/related-topics/viral-hepatitis-very-real-consequence-substance-use

What are other health effects of anabolic steroids
Aside from mental effects, steroid use commonly causes severe acne. It also causes the body to swell, especially in the hands and feet.
Long-Term Effects
Anabolic steroid misuse might lead to serious, even permanent, health problems such as:

- kidney problems or failure
- liver damage and tumors
- enlarged heart, high blood pressure, and changes in blood cholesterol, all of which increase the risk of stroke and heart attack, even in young people
- increased risk of blood clots

Several other effects are gender- and age-specific:
In men:

- shrinking testicles
- decreased sperm count
- baldness
- development of breasts
- increased risk for prostate cancer

In women*:*

- growth of facial hair or excess body hair
- decreased breast size
- male-pattern baldness
- changes in or stop in the menstrual cycle
- enlarged clitoris
- deepened voice

In teens:

- stunted growth (when high hormone levels from steroids signal to the body to stop bone growth too early)
- stunted height (if teens use steroids before their growth spurt)

Some of these physical changes, such as shrinking sex organs in men, can add to mental side effects such as mood disorders.

Are anabolic steroids addictive?
Even though anabolic steroids do not cause the same high as other drugs, they can lead to a substance use disorder. A substance use disorder occurs when a person continues to misuse steroids, even though there are serious consequences for doing so. The most severe form of a substance use disorder is addiction. People might continue to misuse steroids despite physical problems, high costs to buy the drugs, and negative effects on their relationships. These behaviors reflect steroids' addictive potential. Research has further found that some steroid users turn to other drugs, such as opioids, to reduce sleep problems and irritability caused by steroids.

People who misuse steroids might experience withdrawal symptoms when they stop use, including:

- fatigue
- restlessness
- loss of appetite
- sleep problems
- decreased sex drive
- steroid cravings

One of the more serious withdrawal symptoms is depression, which can sometimes lead to suicide attempts.

How can people get treatment for anabolic steroid addiction?
Some people seeking treatment for anabolic steroid addiction have found a combination of behavioral therapy and medications to be helpful.

In certain cases of addiction, patients have taken medicines to help treat symptoms of withdrawal. For example, health care providers have prescribed antidepressants to treat depression and pain medicines for headaches and muscle and joint pain. Other medicines have been used to help restore the patient's hormonal system.

Points to Remember

- Anabolic steroids are synthetic variations of the male sex hormone testosterone.
- Health care providers can prescribe steroids to treat various medical conditions. But some athletes and bodybuilders misuse these drugs to boost performance or improve their physical appearance.
- People who abuse anabolic steroids usually take them orally, inject them into the muscles, or apply them to the skin with a cream or gel.
- People misuse steroids in a variety of doses and schedules.
- Misuse of anabolic steroids might lead to short-term effects, including paranoid jealousy, extreme irritability and aggression, delusions, impaired judgement, and mania.
- Continued steroid misuse can act on some of the same brain pathways and chemicals that are affected by other drugs, including dopamine, serotonin, and opioid systems.
- Anabolic steroid misuse might lead to serious long-term, even permanent, health problems.
- Several other effects are gender- and age-specific.

- People who inject steroids increase their risk of contracting or transmitting HIV/AIDS or hepatitis.
- Even though anabolic steroids do not cause the same high as other drugs, they can lead to addiction.
- Some people seeking treatment for anabolic steroid addiction have found behavioral therapy and medications to be helpful. Medicines can help treat symptoms of withdrawal in some cases.

B. Cigarettes and Other Tobacco Products

What is tobacco?

Tobacco is a plant grown for its leaves, which are dried and fermented before being put in tobacco products. Tobacco contains nicotine, an ingredient that can lead to addiction, which is why so many people who use tobacco find it difficult to quit. There are also many other potentially harmful chemicals found in tobacco or created by burning it.

How do people use tobacco?

People can smoke, chew, or sniff tobacco. Smoked tobacco products include cigarettes, cigars, bidis, and kreteks. Some people also smoke loose tobacco in a pipe or hookah (water pipe). Chewed tobacco products include chewing tobacco, snuff, dip, and snus; snuff can also be sniffed.

How does tobacco affect the brain?

The nicotine in any tobacco product readily absorbs into the blood when a person uses it. Upon entering the blood, nicotine immediately stimulates the adrenal glands to release the hormone epinephrine (adrenaline). Epinephrine stimulates the central nervous system and increases blood pressure, breathing, and heart rate. As with drugs such as cocaine and heroin, nicotine activates the brain's reward circuits and also increases levels of the chemical messenger *dopamine*, which reinforces rewarding behaviors. Studies suggest that other chemicals in tobacco smoke, such as acetaldehyde, may enhance nicotine's effects on the brain.

What are other health effects of tobacco use?

Although nicotine is addictive, most of the severe health effects of tobacco use comes from other chemicals. Tobacco smoking can lead to lung cancer, chronic bronchitis, and emphysema. It increases the risk of heart disease, which can lead to stroke or heart attack. Smoking has also been linked to other cancers, leukemia, cataracts, Type 2 Diabetes, and pneumonia. All of these risks apply to use of any smoked product, including hookah tobacco. Smokeless tobacco increases the risk of cancer, especially mouth cancers.

Pregnant women who smoke cigarettes run an increased risk of miscarriage, stillborn or premature infants, or infants with low birth weight. Smoking while pregnant may also be associated with learning and behavioral problems in exposed children.

People who stand or sit near others who smoke are exposed to secondhand smoke, either coming from the burning end of the tobacco product or exhaled by the person who is smoking. Secondhand smoke exposure can also lead to lung cancer and heart disease. It can cause health problems in both adults and children, such as coughing, phlegm, reduced lung function, pneumonia, and bronchitis. Children exposed to secondhand smoke are at an increased risk of ear infections, severe asthma, lung infections, and death from sudden infant death syndrome.

Electronic Cigarettes

Electronic cigarettes, also known as e-cigarettes or e-vaporizers, are battery-operated devices that deliver nicotine with flavorings and other chemicals to the lungs in vapor instead of smoke. E-cigarette companies often advertise them as safer than traditional cigarettes because they don't burn tobacco. But researchers actually know little about the health risks of using these devices.

How does tobacco use lead to addiction?

For many who use tobacco, long-term brain changes brought on by continued nicotine exposure result in addiction. When a person tries to quit, he or she may have withdrawal symptoms, including:

- irritability
- problems paying attention
- trouble sleeping
- increased appetite
- powerful cravings for tobacco

How can people get treatment for nicotine addiction?
Both behavioral treatments and medications can help people quit smoking, but the combination of medication with counseling is more effective than either alone.

The U.S. Department of Health and Human Services has established a national toll-free quitline, 1-800-QUIT-NOW, to serve as an access point for anyone seeking information and help in quitting smoking.

Behavioral Treatments

Government Regulation of Tobacco Products
On May 5, 2016, the FDA announced that nationwide tobacco regulations now extend to *all* tobacco products, including:

- e-cigarettes and their liquid solutions
- cigars
- hookah tobacco
- pipe tobacco

This ruling includes restricting sale of these products to minors. For more information, see the FDA's webpage, The Facts on the FDA's New Tobacco Rule.
Behavioral treatments use a variety of methods to help people quit smoking, ranging from self-help materials to counseling. These treatments teach people to recognize high-risk situations and develop strategies to deal with them. For example, people who hang out with others who smoke are more likely to smoke and less likely to quit.

Nicotine Replacement Therapies

Nicotine replacement therapies (NRTs) were the first medications the U.S. Food and Drug Administration (FDA) approved for use in smoking cessation therapy.

Current FDA-approved NRT products include chewing gum, transdermal patch, nasal sprays, inhalers, and lozenges. NRTs deliver a controlled dose of nicotine to relieve withdrawal symptoms while the person tries to quit.

Other Medications

Bupropion (Zyban®) and varenicline (Chantix®) are two FDA-approved non-nicotine medications that have helped people quit smoking. They target nicotine

receptors in the brain, easing withdrawal symptoms and blocking the effects of nicotine if people start smoking again.

Reports of Deaths Related to Vaping

The Food and Drug Administration has alerted the public to hundreds of reports of serious lung illnesses associated with vaping, including several deaths. They are working with the Centers for Disease Control and Prevention (CDC) to investigate the cause of these illnesses. Many of the suspect products tested by the states or federal health officials have been identified as vaping products containing THC, the main psychotropic ingredient in marijuana. Some of the patients reported a mixture of THC and nicotine; and some reported vaping nicotine alone. No one substance has been identified in all of the samples tested, and it is unclear if the illnesses are related to one single compound. Until more details are known, FDA officials have warned people not to use any vaping products bought on the street, and they warn against modifying any products purchased in stores. They are also asking people and health professionals to report any adverse effects. The CDC has posted an information page for consumers.

Can a person overdose on nicotine?

Nicotine is poisonous and, though uncommon, overdose is possible. An overdose occurs when the person uses too much of a drug and has a toxic reaction that results in serious, harmful symptoms or death. Nicotine poisoning usually occurs in young children who accidentally chew on nicotine gum or patches used to quit smoking or swallow e-cigarette liquid. Symptoms include difficulty breathing, vomiting, fainting, headache, weakness, and increased or decreased heart rate. Anyone concerned that a child or adult might be experiencing a nicotine overdose should seek immediate medical help.

Points to Remember

- Tobacco is a plant grown for its leaves, which are dried and fermented before being put in tobacco products. Tobacco contains nicotine, the ingredient that can lead to addiction.
- People can smoke, chew, or sniff tobacco.
- Nicotine acts in the brain by stimulating the adrenal glands to release the hormone epinephrine (adrenaline) and by increasing levels of the chemical messenger dopamine.
- Tobacco smoking can lead to lung cancer, chronic bronchitis, and emphysema. It increases the risk of heart disease, which can lead to stroke or heart attack. Smoking has also been linked to other cancers, leukemia, cataracts, and pneumonia. Smokeless tobacco increases the risk of cancer, especially mouth cancers.
- Secondhand smoke can lead to lung cancer and heart disease as well as other health effects in adults and children.
- For many who use tobacco, long-term brain changes brought on by continued nicotine exposure result in addiction.
- Both behavioral treatments and medication can help people quit smoking, but the combination of medication with counseling is more effective than either alone.
- Nicotine overdose is possible, though it usually occurs in young children who accidentally chew on nicotine gum or patches or swallow e-cigarette liquid.

• Anyone concerned that a child or adult might be experiencing a nicotine overdose should seek immediate medical help.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.
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C. Cocaine

What is cocaine?

Cocaine is a powerfully addictive stimulant drug made from the leaves of the coca plant native to South America. Although health care providers can use it for valid medical purposes, such as local anesthesia for some surgeries, recreational cocaine use is illegal. As a street drug, cocaine looks like a fine, white, crystal powder. Street dealers often mix it with things like cornstarch, talcum powder, or flour to increase profits. They may also mix it with other drugs such as the stimulant amphetamine, or synthetic opioids, including fentanyl. Adding synthetic opioids to cocaine is especially risky when people using cocaine don't realize it contains this dangerous additive. Increasing numbers of overdose deaths among cocaine users might be related to this tampered cocaine.
Popular nicknames for cocaine include:

- Blow
- Coke
- Crack
- Rock
- Snow

How do people use cocaine?

People snort cocaine powder through the nose, or they rub it into their gums. Others dissolve the powder and inject it into the bloodstream. Some people inject a combination of cocaine and heroin, called a Speedball.

Another popular method of use is to smoke cocaine that has been processed to make a rock crystal (also called "freebase cocaine"). The crystal is heated to produce vapors that are inhaled into the lungs. This form of cocaine is called Crack, which refers to the crackling sound of the rock as it's heated. Some people also smoke Crack by sprinkling it on marijuana or tobacco, and smoke it like a cigarette.

People who use cocaine often take it in binges—taking the drug repeatedly within a short time, at increasingly higher doses—to maintain their high.

How does cocaine affect the brain?

Cocaine increases levels of the natural chemical messenger *dopamine in* brain circuits related to the control of movement and reward.

Normally, dopamine recycles back into the cell that released it, shutting off the signal between nerve cells. However, cocaine prevents dopamine from being recycled, causing large amounts to build up in the space between two nerve cells, stopping their normal communication. This flood of dopamine in the brain's reward circuit strongly reinforces drug-taking behaviors, because the reward circuit eventually adapts to the excess of dopamine caused by cocaine, and becomes less sensitive to it. As a result, people take stronger and more frequent doses in an attempt to feel the same high, and to obtain relief from withdrawal.

Short-Term Effects
Short-term health effects of cocaine include:

- extreme happiness and energy
- mental alertness
- hypersensitivity to sight, sound, and touch
- irritability
- *paranoia*—extreme and unreasonable distrust of others

Some people find that cocaine helps them perform simple physical and mental tasks more quickly, although others experience the opposite effect. Large amounts of cocaine can lead to bizarre, unpredictable, and violent behavior.

Cocaine's effects appear almost immediately and disappear within a few minutes to an hour. How long the effects last and how intense they are depend on the method of use. Injecting or smoking cocaine produces a quicker and stronger but shorter-lasting high than snorting. The high from snorting cocaine may last 15 to 30 minutes. The high from smoking may last 5 to 10 minutes.

What are other health effects of cocaine use?
Other health effects of cocaine use include:

- constricted blood vessels
- dilated pupils
- nausea
- raised body temperature and blood pressure
- fast or irregular heartbeat
- tremors and muscle twitches
- restlessness

Long-Term Effects
Some long-term health effects of cocaine depend on the method of use and include the following:

- *snorting:* loss of smell, nosebleeds, frequent runny nose, and problems with swallowing
- *smoking:* cough, asthma, respiratory distress, and higher risk of infections like pneumonia
- *consuming by mouth:* severe bowel decay from reduced blood flow

- *needle injection:* higher risk for contracting HIV, hepatitis C, and other bloodborne diseases, skin or soft tissue infections, as well as scarring or collapsed veins

However, even people involved with non-needle cocaine use place themselves at a risk for HIV because cocaine impairs judgment, which can lead to risky sexual behavior with infected partners.
Other long-term effects of cocaine use include being malnourished, because cocaine decreases appetite, and movement disorders, including Parkinson's disease, which may occur after many years of use. In addition, people report
irritability and restlessness from cocaine binges, and some also experience severe paranoia, in which they lose touch with reality and have *auditory hallucinations*—hearing noises that aren't real.

Cocaine, HIV, and Hepatitis
Studies have shown that cocaine use speeds up HIV infection. According to research, cocaine impairs immune cell function and promotes reproduction of the HIV virus. Research also suggests that people who use cocaine and are infected with HIV may be more susceptible to contracting other viruses, such as hepatitis C, a virus that affects the liver.
Read more about the connection between cocaine and these diseases in NIDA's *Cocaine Research Report:* drugabuse.gov/publications/research-reports/cocaine/what-cocaine.

Can a person overdose on cocaine?
Yes, a person can overdose on cocaine. An overdose occurs when a person uses enough of a drug to produce serious adverse effects, life-threatening symptoms, or death. An overdose can be intentional or unintentional.

Death from overdose can occur on the first use of cocaine or unexpectedly thereafter. Many people who use cocaine also drink alcohol at the same time, which is particularly risky and can lead to overdose. Others mix cocaine with heroin, another dangerous—and deadly—combination.

Some of the most frequent and severe health consequences of overdose are irregular heart rhythm, heart attacks, seizures, and strokes. Other symptoms of cocaine overdose include difficulty breathing, high blood pressure, high body temperature, hallucinations, and extreme agitation or anxiety.

How can a cocaine overdose be treated?
There is no specific medication that can reverse a cocaine overdose. Management involves supportive care and depends on the symptoms present. For instance, because cocaine overdose often leads to a heart attack, stroke, or seizure, first responders and emergency room doctors try to treat the overdose by treating these conditions, with the intent of:

- restoring blood flow to the heart (heart attack)
- restoring oxygen-rich blood supply to the affected part of the brain (stroke)

- stopping the seizure

How does cocaine use lead to addiction?

As with other drugs, repeated use of cocaine can cause long-term changes in the brain's reward circuit and other brain systems, which may lead to addiction. The reward circuit eventually adapts to the extra dopamine caused by the drug, becoming steadily less sensitive to it. As a result, people take stronger and more frequent doses to feel the same high they did initially and to obtain relief from withdrawal.

Withdrawal symptoms include:

- depression
- fatigue
- increased appetite
- unpleasant dreams and insomnia
- slowed thinking

How can people get treatment for cocaine addiction?

Behavioral therapy may be used to treat cocaine addiction. Examples include:

- cognitive-behavioral therapy
- contingency management or motivational incentives—providing rewards to patients who remain substance free
- therapeutic communities—drug-free residences in which people in recovery from substance use disorders help each other to understand and change their behaviors
- community based recovery groups, such as 12-step programs

While no government-approved medicines are currently available to treat cocaine addiction, researchers are testing some treatments that have been used to treat other disorders, including:

- disulfiram (used to treat alcoholism)
- modanifil (used to treat *narcolepsy*—a disorder characterized by uncontrollable episodes of deep sleep)
- lorcaserin (used to treat obesity)
- buprenorphine (used to treat opioid addiction)

Points to Remember

- Cocaine is a powerfully addictive stimulant drug made from the leaves of the coca plant native to South America.
- Street dealers often mix it with things like cornstarch, talcum powder, or flour to increase profits.
- They may also mix it with other drugs such as the stimulant amphetamine or the synthetic opioid fentanyl.
- People snort cocaine powder through the nose, or rub it into their gums. Others dissolve the powder and inject it into the bloodstream, or inject a combination of cocaine and heroin, called a Speedball. Another popular method of use is to smoke Crack cocaine.

- Cocaine increases levels of the natural chemical messenger dopamine in brain circuits related to the control of movement and reward.
- A person can overdose on cocaine, which can lead to death.
- Behavioral therapy may be used to treat cocaine addiction.
- While no government-approved medicines are currently available to treat cocaine addiction, researchers are testing some treatments that have been used to treat other disorders.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.
Updated July 2018

D. Fentanyl

What is fentanyl?

Fentanyl is a powerful synthetic opioid that is similar to morphine but is 50 to 100 times more potent.[1] [2] It is a prescription drug that is also made and used illegally. Like morphine, it is a medicine that is typically used to treat patients with severe pain, especially after surgery.[3] It is also sometimes used to treat patients with chronic pain who are physically tolerant to other opioids.[4] Tolerance occurs when you need a higher and/or more frequent amount of a drug to get the desired effects.

In its prescription form, fentanyl is known by such names as Actiq®, Duragesic®, and Sublimaze®.[5] Street names for illegally used fentanyl include Apache, China Girl, China White, Dance Fever, Friend, Goodfellas, Jackpot, Murder 8, and Tango & Cash.

Synthetic opioids, including fentanyl, are now the most common drugs involved in drug overdose deaths in the United States. In 2017, 59.8 percent of opioid-related deaths involved fentanyl compared to 14.3 percent in 2010.

What are Opioids?

Opioids are a class of drugs naturally found in the opium poppy plant. Some opioids are made from the plant directly, and others, like fentanyl, are made by scientists in labs using the same chemical structure (semi-synthetic or synthetic).

How do people use fentanyl?

When prescribed by a doctor, fentanyl can be given as a shot, a patch that is put on a person's

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[1] . Volpe DA, Tobin GAM, Mellon RD, et al. Uniform assessment and ranking of opioid Mu receptor binding constants for selected opioid drugs. *Regul Toxicol Pharmacol*. 2011;59(3):385-390. doi:10.1016/j.yrtph.2010.12.007

[2] Higashikawa Y, Suzuki S. Studies on 1-(2-phenethyl)-4-(N-propionylanilino)piperidine (fentanyl) and its related compounds. VI. Structure-analgesic activity relationship for fentanyl, methyl-substituted fentanyls and other analogues. *Forensic Toxicol*. 2008;26(1):1-5. doi:10.1007/s11419-007-0039-1

[3] . Nelson L, Schwaner R. Transdermal fentanyl: Pharmacology and toxicology. *J Med Toxicol*. 2009;5(4):230-241. doi:10.1007/BF03178274

[4] Garnock-Jones KP. Fentanyl Buccal Soluble Film: A Review in Breakthrough Cancer Pain. *Clin Drug Investig*. 2016;36(5):413-419. doi:10.1007/s40261-016-0394-y

[5] Drug and Chemical Evaluation Section, Office of Diversion Control, Drug Enforcement Administration. Fentanyl Fact Sheet. March 2015. http://www.deadiversion.usdoj.gov/drug_chem_info/fentanyl.pdf.

skin, or as lozenges that are sucked like cough drops.[6]
The illegally used fentanyl most often associated with recent overdoses is made in labs. This synthetic fentanyl is sold illegally as a powder, dropped onto blotter paper, put in eye droppers and nasal sprays, or made into pills that look like other prescription opioids.[7]

Some drug dealers are mixing fentanyl with other drugs, such as heroin, cocaine, methamphetamine, and MDMA. This is because it takes very little to produce a high with fentanyl, making it a cheaper option. This is especially risky when people taking drugs don't realize they might contain fentanyl as a cheap but dangerous additive. They might be taking stronger opioids than their bodies are used to and can be more likely to overdose.

How does fentanyl affect the brain?
Like heroin, morphine, and other opioid drugs, fentanyl works by binding to the body's opioid receptors, which are found in areas of the brain that control pain and emotions.[8] After taking opioids many times, the brain adapts to the drug, diminishing its sensitivity, making it hard to feel pleasure from anything besides the drug. When people become addicted, drug seeking and drug use take over their lives.
Fentanyl's effects include

- • extreme happiness
- • drowsiness
- • nausea
- • confusion
- • constipation
- • sedation
- • problems breathing
- • unconsciousness

Can you overdose on fentanyl?
Yes, a person can overdose on fentanyl. An overdose occurs when a drug produces serious adverse effects and life-threatening symptoms. When people overdose on fentanyl, their breathing can slow or stop. This can decrease the amount of oxygen that reaches the brain, a condition called *hypoxia.* Hypoxia can lead to a coma and permanent brain damage, and even death.

How can a fentanyl overdose be treated?
As mentioned above, many drug dealers mix the cheaper fentanyl with other drugs like heroin, cocaine, MDMA and methamphetamine to increase their profits, making it often difficult to know which drug is causing the overdose. Naloxone is a medicine that can treat a fentanyl overdose

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[6] American Academy of Pediatrics Committee on Drugs. Transfer of drugs and other chemicals into human milk. *Pediatrics*. 2001;108(3):776-789.
[7] Drug and Chemical Evaluation Section, Office of Diversion Control, Drug Enforcement Administration. Acetyl fentanyl Fact Sheet. July 2015. http://www.deadiversion.usdoj.gov/drug_chem_info/acetylfentanyl.pdf.
[8] Gutstein H, Akil H. Opioid Analgesics. In: *Goodman & Gilman's the Pharmacological Basis of Therapeutics*. 11th ed. McGraw-Hill; 2006:547-590.

when given right away. It works by rapidly binding to opioid receptors and blocking the effects of opioid drugs. But fentanyl is stronger than other opioid drugs like morphine and might require multiple doses of naloxone.
Because of this, if you suspect someone has overdosed, the most important step to take is to call 911 so he or she can receive immediate medical attention. Once medical personnel arrive, they will administer naloxone if they suspect an opioid drug is involved.

People who are given naloxone should be monitored for another two hours after the last dose of naloxone is given to make sure breathing does not slow or stop.

Some states have passed laws that allow pharmacists to dispense naloxone without a personal prescription. This allows friends, family, and others in the community to use the auto-injector or nasal spray versions of naloxone to save someone who is overdosing. People who are or know someone at risk for an opioid overdose can be trained on how to give naloxone and can carry it with them in case of an emergency.

Naloxone is available as an injectable (needle) solution, a hand-held auto-injector (EVZIO®), and a nasal spray (NARCAN® Nasal Spray).

Can fentanyl use lead to addiction?
Yes. Fentanyl is addictive because of its potency. A person taking prescription fentanyl as instructed by a doctor can experience dependence, which is characterized by withdrawal symptoms when the drug is stopped. A person can be dependent on a substance without being addicted, but dependence can sometimes lead to addiction.

Addiction is the most severe form of a *substance use disorder* (SUD). SUDs are characterized by compulsive drug seeking and drug use that can be difficult to control, despite harmful consequences. When someone is addicted to drugs, they continue to use them even though they cause health problems or issues at work, school, or home. An SUD can range from mild to severe.

People addicted to fentanyl who stop using it can have severe withdrawal symptoms that begin as early as a few hours after the drug was last taken. These symptoms include:

- muscle and bone pain
- sleep problems
- diarrhea and vomiting
- cold flashes with goose bumps
- uncontrollable leg movements
- severe cravings

These symptoms can be extremely uncomfortable and are the reason many people find it so difficult to stop taking fentanyl. There are medicines being developed to help with the withdrawal process for fentanyl and other opioids. The FDA has approved lofexidine, a non-opioid medicine designed to reduce opioid withdrawal symptoms. Also, the NSS-2 Bridge device

is a small electrical nerve stimulator placed behind the person's ear, that can be used to try to ease symptoms for up to five days during the acute withdrawal phase. In December 2018, the FDA cleared a mobile medical application, reSET®, to help treat opioid use disorders. This application is a prescription cognitive behavioral therapy and should be used in conjunction with treatment that includes buprenorphine and contingency management.

How is fentanyl addiction treated?
Like other opioid addictions, medication with behavioral therapies has been shown to be effective in treating people with a fentanyl addiction.

Medications: Buprenorphine and methadone work by binding to the same opioid receptors in the brain as fentanyl, reducing cravings and withdrawal symptoms. Another medicine, naltrexone, blocks opioid receptors and prevents fentanyl from having an effect. People can discuss treatment options with their health provider.

Counseling: Behavioral therapies for addiction to opioids like fentanyl can help people modify their attitudes and behaviors related to drug use, increase healthy life skills, and help them stick with their medication. Some examples include:

- cognitive behavioral therapy, which helps modify the patient's drug use expectations and behaviors, and effectively manage triggers and stress
- contingency management, which uses a voucher-based system giving patients "points" based on negative drug tests. They can use the points to earn items that encourage healthy living
- Motivational interviewing, which is a patient-centered counseling style that addresses a patient's mixed feelings to change

These behavioral treatment approaches have proven effective, especially when used along with medicines.

Points to Remember

- Fentanyl is a powerful synthetic opioid analgesic that is similar to morphine but is 50 to 100 times more potent. In its prescription form it is prescribed for pain, but fentanyl is also made illegally and distributed as a street drug.
- Fentanyl and other synthetic opioids are the most common drugs involved in overdose deaths.
- Illegal fentanyl is sold in the following forms: as a powder, dropped on blotter paper like small candies, in eye droppers or nasal sprays, or made into pills that look like real prescription opioids.

- Illegal fentanyl is being mixed with other drugs, such as cocaine, heroin, methamphetamine, and MDMA. This is especially dangerous because people are often unaware that fentanyl has been added.
- Fentanyl works by binding to the body's opioid receptors, which are found in areas of the brain that control pain and emotions. Its effects include extreme happiness, drowsiness, nausea, confusion, constipation, sedation, tolerance, addiction, respiratory depression and arrest, unconsciousness, coma, and death.
- The high potency of fentanyl greatly increases risk of overdose, especially if a person who uses drugs is unaware that a powder or pill contains it. They can underestimate the dose of opioids they are taking, resulting in overdose.
- Naloxone is a medicine that can be given to a person to reverse a fentanyl overdose. Multiple naloxone doses might be necessary because of fentanyl's potency.
- Medication with behavioral therapies has been shown to be effective in treating people with an addiction to fentanyl and other opioids.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.

This page was last updated February 2019

E. Hallucinogens

What are hallucinogens?

Hallucinogens are a diverse group of drugs that alter a person's awareness of their surroundings as well as their own thoughts and feelings. They are commonly split into two categories: **classic hallucinogens** (such as LSD) and **dissociative drugs** (such as PCP). Both types of hallucinogens can cause *hallucinations,* or sensations and images that seem real though they are not. Additionally, dissociative drugs can cause users to feel out of control or disconnected from their body and environment.

Some hallucinogens are extracted from plants or mushrooms, and some are synthetic (human-made). Historically, people have used hallucinogens for religious or healing rituals. More recently, people report using these drugs for social or recreational purposes, including to have fun, deal with stress, have spiritual experiences, or just to feel different.

Common classic hallucinogens include the following:

• **LSD *(D-lysergic acid diethylamide)*** is one of the most powerful mind-altering chemicals. It is a clear or white odorless material made from lysergic acid, which is found in a fungus that grows on rye and other grains. LSD has many other street names, including acid, blotter acid, dots, and mellow yellow.

• **Psilocybin *(4-phosphoryloxy-N,N-dimethyltryptamine)*** comes from certain types of mushrooms found in tropical and subtropical regions of South America, Mexico, and the United States. Some common names for psilocybin include little smoke, magic mushrooms, and shrooms.

- **Peyote (mescaline)** is a small, spineless cactus with mescaline as its main ingredient. Peyote can also be synthetic. Common names for peyote are buttons, cactus, and mesc.

- **DMT (*N,N-dimethyltryptamine*)** is a powerful chemical found naturally in some Amazonian plants. Ayahuasca is a tea made from such plants, and when taken in this form it is also known as hoasca, aya, and yagé. People can also make DMT in a lab. Synthetic DMT usually takes the form of a white crystalline powder that is smoked. A popular name for synthetic DMT is Dimitri.

- **251-NBOMe** is a synthetic hallucinogen with similarities both to LSD and MDMA (see DrugFacts: MDMA) but that is much more potent. Developed for use in brain research, when sold on the street it is sometimes called N Bomb or 251.

Common examples of dissociative drugs include the following:

• **PCP *(Phencyclidine)*** was developed in the 1950s as a general anesthetic for surgery, but it is no longer used for this purpose due to serious side effects. PCP can be found in a variety of forms, including tablets or capsules; however, liquid and white crystal powder are the most common. PCP has various slang names, such as Angel Dust, Hog, Love Boat, and Peace Pill.

• **Ketamine** is used as a surgery anesthetic for humans and animals. Much of the ketamine sold on the streets comes from veterinary offices. It mostly sells as a powder or as pills, but it also available as an injectable liquid. Ketamine is snorted or sometimes added to drinks as a date-rape drug. Slang names for ketamine include Special K and Cat Valium.

• ***Dextromethorphan*** **(DXM)** is a cough suppressant and mucus-clearing ingredient in some over-the-counter cold and cough medicines (syrups, tablets, and gel capsules). Robo is a common slang name for DXM.

• ***Salvia (Salvia divinorum)*** is a plant common to southern Mexico and Central and South America. Salvia is typically ingested by chewing fresh leaves or by drinking their extracted juices. The dried leaves of salvia can also be smoked or vaporized and inhaled. Popular names for salvia are Diviner's Sage, Maria Pastora, Sally-D, and Magic Mint.

How do people use hallucinogens?

People use hallucinogens in a wide variety of ways, as shown in the following chart:

	DMT	LSD	Peyote	Psilocybin	DXM	Ketamine	PCP	Salvia
Swallowing as tablets or pills		√			√	√	√	
Swallowing as liquid		√	√		√	√		
Consuming raw or dried			√	√				√
Brewing into Tea	√		√	√				√
Snorting						√	√	
Injecting							√	
Inhaling, vaporizing, or smoking	√						√	√
Absorbing through the lining in the mouth using drug-soaked paper pieces		√						

How do hallucinogens affect the brain?

Research suggests that classic hallucinogens work at least partially by temporarily disrupting communication between brain chemical systems throughout the brain and spinal cord. Some hallucinogens interfere with the action of the brain chemical serotonin, which regulates:

- mood
- sensory perception
- sleep
- hunger
- body temperature
- sexual behavior
- intestinal muscle control

Dissociative hallucinogenic drugs interfere with the action of the brain chemical glutamate, which regulates:

- pain perception
- responses to the environment
- emotion
- learning and memory

What are some other effects of hallucinogens?

Classic Hallucinogens

Short-Term Effects

Classic hallucinogens can cause users to see images, hear sounds, and feel sensations that seem real but do not exist. The effects generally begin within 20 to 90 minutes and can last as long as 12 hours in some cases (LSD) or as short as 15 minutes in others (synthetic DMT). Hallucinogen users refer to the experiences brought on by these drugs as "trips." If the experience is unpleasant, users sometimes call it a "bad trip."

Along with hallucinations, other short-term general effects include:

- increased heart rate
- nausea
- intensified feelings and sensory experiences (such as seeing brighter colors)
- changes in sense of time (for example, the feeling that time is passing by slowly)

Specific short-term effects of some hallucinogens include:

- increased blood pressure, breathing rate, or body temperature
- loss of appetite
- dry mouth

- sleep problems
- spiritual experiences
- feelings of relaxation
- uncoordinated movements
- excessive sweating
- panic
- *paranoia*—extreme and unreasonable distrust of others
- *psychosis*—disordered thinking detached from reality
- bizarre behaviors

Long-Term Effects
Two long-term effects have been associated with use of classic hallucinogens, although these effects are rare.

• ***Persistent Psychosis—***a series of continuing mental problems, including:
- visual disturbances
- disorganized thinking
- paranoia
- mood changes

• ***Hallucinogen Persisting Perception Disorder (HPDD)—***recurrences of certain drug experiences, such as hallucinations or other visual disturbances. These flashbacks often happen without warning and may occur within a few days or more than a year after drug use. These symptoms are sometimes mistaken for other disorders, such as stroke or a brain tumor.

Both conditions are seen more often in people who have a history of mental illness, but they can happen to anyone, even after using hallucinogens one time. For HPDD, some antidepressant and antipsychotic medications can be used to improve mood and treat psychosis. Behavioral therapies can be used to help people cope with fear or confusion associated with visual disturbances.

Dissociative Drugs
Short-Term Effects

Dissociative drug effects can appear within a few minutes and can last several hours in some cases; some users report experiencing drug effects for days.

Effects depend on how much is used. In low and moderate doses, dissociative drugs can cause:

- numbness
- disorientation and loss of coordination
- hallucinations
- increase in blood pressure, heart rate, and body temperature

In high doses, dissociative drugs can cause the following effects:

- memory loss
- panic and anxiety
- seizures
- psychotic symptoms
- amnesia
- inability to move
- mood swings
- trouble breathing

Long-Term Effects of Dissociative Drugs

More research is needed on the long-term effects of dissociative drugs. Researchers do know repeated use of PCP can result in addiction. Other long-term effects may continue for a year or more after use stops, including:

- speech problems
- memory loss
- weight loss
- anxiety
- depression and suicidal thoughts

Effects on a Developing Fetus

While the effects of most hallucinogens on the developing fetus are unknown, researchers do know that mescaline in peyote may affect the fetus of a pregnant woman using the drug.

Can a person overdose on hallucinogens?

It depends on the drug. An overdose occurs when a person uses enough of a drug to produce serious adverse effects, life-threatening symptoms, or death. Most classic hallucinogens may produce extremely unpleasant experiences at high doses, although the effects are not necessarily

life-threatening. However, serious medical emergencies and several fatalities have been reported from 251-NBOMe.

Overdose is more likely with some dissociative drugs. High doses of PCP can cause seizures, coma, and death. Additionally, taking PCP with depressants such as alcohol or benzodiazepines can also lead to coma. Benzodiazepines, such as alprazolam (Xanax), are prescribed to relieve anxiety or promote sleep.

However, users of both classic hallucinogens and dissociative drugs also risk serious harm because of the profound alteration of perception and mood these drugs can cause.

- Users might do things they would never do in real life, like jump out of a window or off a roof, for instance, or they may experience profound suicidal feelings and act on them.
- With all drugs there is also a risk of accidental poisoning from contaminants or other substances mixed with the drug.
- Users of psilocybin also run the risk of accidentally consuming poisonous mushrooms that look like psilocybin. Taking poisonous mushrooms can result in severe illness or possible death.

Are hallucinogens addictive?

In some cases, yes. Evidence suggests that certain hallucinogens can be addictive, and that people can develop a tolerance to them.

For example, LSD is not considered an addictive drug because it doesn't cause uncontrollable drug-seeking behavior. However, LSD does produce tolerance, so some users who take the drug repeatedly must take higher doses to achieve the same effect. This is an extremely dangerous practice, given the unpredictability of the drug. In addition, LSD produces tolerance to other hallucinogens, including psilocybin.

The misuse and addiction potential of DMT is currently unknown. Unlike other hallucinogens, DMT does not appear to lead to tolerance. There is also little evidence that taking it in the form of ayahuasca tea can lead to addiction.

On the other hand, PCP is a hallucinogen that can be addictive. People who stop repeated use of PCP experience drug cravings, headaches, and sweating as common withdrawal symptoms.

More research is needed on the tolerance or addiction potential of a variety of hallucinogens.

Tolerance vs. Dependence vs. Addiction

Long-term use of prescription opioids, even as prescribed by a doctor, can cause some people to develop a **tolerance**, which means that they need higher and/or more frequent doses of the drug to get the desired effects.

Drug dependence occurs with repeated use, causing the neurons to adapt so they only function normally in the presence of the drug. The absence of the drug causes several physiological reactions, ranging from mild in the case of caffeine, to potentially life-threatening, such as with heroin. Some chronic pain patients are dependent on opioids and require medical support to stop taking the drug.

Drug addiction is a chronic disease characterized by compulsive, or uncontrollable, drug seeking and use despite harmful consequences and long-lasting changes in the brain. The changes can result in harmful behaviors by those who misuse drugs, whether prescription or illicit drugs.

How is a hallucinogen addiction treated?

There are no FDA-approved medications to treat addiction to hallucinogens. While behavioral treatments can be helpful for patients with a variety of addictions, scientists need more research to find out if behavioral therapies are effective for addiction to hallucinogens.

Could hallucinogens be medicines?

Potentially. Some hallucinogens have been studied for possible therapeutic benefits in treating mental disorders such as depression.

Ketamine was approved many years ago as an anesthetic for painful medical procedures. In March 2019, the medicine esketamine (called “Spravato” by the manufacturer) was approved by the Food and Drug Administration as a treatment for severe depression in patients that do not respond to other treatments. Esketamine is closely related to the drug ketamine which is used illicitly and so there are concerns about the potential for abuse of this newly approved medication. In response, esketamine will be limited to administration in medical facilities.

Unlike a prescription that can be taken home and might be diverted into recreational use, esketamine will be administered in a medical office as a nasal spray. Patients must wait at least 2 hours under medical supervision to ensure proper management of potential side effects. It is a rapid acting medication, so improvements may be seen immediately or within the first few weeks of treatment (unlike most other antidepressants which can take weeks to begin to show an effect). Traditional antidepressants target the neurotransmitters serotonin, norepinephrine or dopamine. Esketamine affects the receptor for a different brain chemical called glutamate and so it represents a new approach to treating depression.

Evidence has also mounted in recent years that psilocybin may be effective in treating depression, and this is currently being studied in clinical trials. Psilocybin is not approved by the Food and Drug Administration (FDA), but in 2018, the FDA granted "Breakthrough Therapy" designation to one pharmaceutical company to facilitate clinical trials for its psilocybin-assisted therapy for treatment-resistant depression; the trials will determine the most optimal dose of the drug. It has also been studied as a possible treatment for depression and anxiety suffered by people with terminal illnesses.

Points to Remember

- Hallucinogens are a diverse group of drugs that alter perception, thoughts, and feelings. They cause hallucinations, or sensations and images that seem real, but they are not.
- Hallucinogens are split into two categories: classic hallucinogens and dissociative drugs.
- People use hallucinogens in a wide variety of ways, including smoking, snorting, and absorbing through the lining in the mouth.
- The effects of classic hallucinogens can begin with 20 to 90 minutes of taking them and include increased heart rate, nausea, intensified feelings and sensory experiences, and changes in sense of time.
- The effects of dissociative drugs can begin within minutes and can last several hours and include numbness, disorientation and loss of coordination, hallucinations, and increased blood pressure, heart rate, and body temperature.
- Persistent psychosis and flashbacks are two long-term effects associated with some hallucinogens.
- Evidence suggests a few hallucinogens can be addictive, and most or all of them can produce tolerance.
- There are no FDA-approved medications to treat addiction to hallucinogens. Scientists need more research to find out if behavioral therapies are effective for addiction to hallucinogens.
- Some hallucinogens are being studied as possible therapies for depression. Esketamine was recently approved by the FDA as a treatment for severe depression in patients that do not respond to other treatments.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.
Updated April 2019

Heroin

What is heroin?

Heroin is an opioid drug made from morphine, a natural substance taken from the seed pod of the various opium poppy plants grown in Southeast and Southwest Asia, Mexico, and Colombia. Heroin can be a white or brown powder, or a black sticky substance known as black tar heroin. Other common names for heroin include *big H*, *horse*, *hell dust,* and *smack*.

How do people use heroin?

People inject, sniff, snort, or smoke heroin. Some people mix heroin with crack cocaine, a practice called *speedballing*.

What are the effects of heroin?

Heroin enters the brain rapidly and binds to opioid receptors on cells located in many areas, especially those involved in feelings of pain and pleasure and in controlling heart rate, sleeping, and breathing.

Prescription Opioids and Heroin

Prescription opioid pain medicines such as OxyContin® and Vicodin® have effects similar to heroin. Research suggests that misuse of these drugs may open the door to heroin use. Data from 2011 showed that an estimated 4 to 6 percent who misuse prescription opioids switch to heroin1-3 and about 80 percent of people who used heroin first misused prescription opioids.[9] [10] [11]More recent data suggest that heroin is frequently the first opioid people use. In a study of those entering treatment for opioid use disorder, approximately one-third reported heroin as the first opioid they used regularly to get high.[12]

This suggests that prescription opioid misuse is just one factor leading to heroin use. Read more about this intertwined problem in our *Prescription Opioids and Heroin Research Report*.

Short-Term Effects

People who use heroin report feeling a "rush" (a surge of pleasure, or euphoria). However, there are other common effects, including:

- dry mouth

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[9] Muhuri PK, Gfroerer JC, Davies MC. Associations of Nonmedical Pain Reliever Use and Initiation of Heroin Use in the United States. CBHSQ Data Rev. August 2013.

[10] Cicero TJ, Ellis MS, Surratt HL, Kurtz SP. The Changing Face of Heroin Use in the United States: A Retrospective Analysis of the Past 50 Years. JAMA Psychiatry. 2014;71(7):821-826. doi:10.1001/jamapsychiatry.2014.366.

[11] Carlson RG, Nahhas RW, Martins SS, Daniulaityte R. Predictors of transition to heroin use among initially non-opioid dependent illicit pharmaceutical opioid users: A natural history study. Drug Alcohol Depend. 2016;160:127-134. doi:10.1016/j.drugalcdep.2015.12.026.

[12] Cicero TJ, Ellis MS, Kasper ZA. Increased use of heroin as an initiating opioid of abuse. Addict Behav. 2017 Nov;74:63-66. doi: 10.1016/j.addbeh.2017.05.030. Epub 2017 May 23. PubMed PMID: 28582659. https://www.ncbi.nlm.nih.gov/pubmed/28582659

- warm flushing of the skin
- heavy feeling in the arms and legs
- nausea and vomiting
- severe itching
- clouded mental functioning
- going "on the nod," a back-and-forth state of being conscious and semiconscious

Long-Term Effects

People who use heroin over the long term may develop:

- insomnia
- collapsed veins for people who inject the drug
- damaged tissue inside the nose for people who sniff or snort it
- infection of the heart lining and valves
- abscesses (swollen tissue filled with pus)
- constipation and stomach cramping
- liver and kidney disease
- lung complications, including pneumonia
- mental disorders such as depression and antisocial personality disorder
- sexual dysfunction for men
- irregular menstrual cycles for women

Other Potential Effects

Heroin often contains additives, such as sugar, starch, or powdered milk, that can clog blood vessels leading to the lungs, liver, kidneys, or brain, causing permanent damage. Also, sharing drug injection equipment and having impaired judgment from drug use can increase the risk of contracting infectious diseases such as HIV and hepatitis (see "Injection Drug Use, HIV, and Hepatitis").

Can a person overdose on heroin?

Yes, a person can overdose on heroin. A heroin overdose occurs when a person uses enough of the drug to produce a life-threatening reaction or death. Heroin overdoses have increased in recent years.[13]

When people overdose on heroin, their breathing often slows or stops. This can decrease the amount of oxygen that reaches the brain, a condition called *hypoxia*. Hypoxia can have short- and

[13] Centers for Disease Control and Prevention (CDC). Multiple Cause of Death, 1999-2015. CDC WONDER Online Database. https://wonder.cdc.gov/mcd-icd10.html. Accessed April 4, 2017.

long-term mental effects and effects on the nervous system, including coma and permanent brain damage.

Injection Drug Use, HIV, and Hepatitis

People who inject drugs such as heroin are at high risk of contracting the HIV and hepatitis C (HCV) virus. These diseases are transmitted through contact with blood or other bodily fluids, which can occur when sharing needles or other injection drug use equipment. HCV is the most common bloodborne infection in the Unites States. HIV (and less often HCV) can also be contracted during unprotected sex, which drug use makes more likely.

Read more about the connection between heroin and these diseases in our *Heroin Research Report*.

How can a heroin overdose be treated?

Naloxone is a medicine that can treat an opioid overdose when given right away. It works by rapidly binding to opioid receptors and blocking the effects of heroin and other opioid drugs. Sometimes more than one dose may be needed to help a person start breathing again, which is why it's important to get the person to an emergency department or a doctor to receive additional support if needed. Read more in the Substance Abuse and Mental Health Services Administration's Opioid Overdose Prevention Toolkit.

Naloxone is available as an injectable (needle) solution, a handheld auto-injector (EVZIO®), and a nasal spray (NARCAN® Nasal Spray). Friends, family, and others in the community can use the auto-injector and nasal spray versions of naloxone to save someone who is overdosing.

The rising number of opioid overdose deaths has led to an increase in public health efforts to make naloxone available to at-risk persons and their families, as well as first responders and others in the community. Some states have passed laws that allow pharmacists to dispense naloxone without a prescription from a person's personal doctor.

Is heroin addictive?

Heroin is highly addictive. People who regularly use heroin often develop a tolerance, which means that they need higher and/or more frequent doses of the drug to get the desired effects. A *substance use disorder* (SUD) is when continued use of the drug causes issues, such as health problems and failure to meet responsibilities at work, school, or home. An SUD can range from mild to severe, the most severe form being addiction.

Those who are addicted to heroin and stop using the drug abruptly may have severe withdrawal. Withdrawal symptoms—which can begin as early as a few hours after the drug was last taken—include:

- restlessness
- severe muscle and bone pain
- sleep problems
- diarrhea and vomiting
- cold flashes with goose bumps ("cold turkey")
- uncontrollable leg movements ("kicking the habit")
- severe heroin cravings

Researchers are studying the long-term effects of opioid addiction on the brain. Studies have shown some loss of the brain's white matter associated with heroin use, which may affect decision-making, behavior control, and responses to stressful situations.[14] [15] [16]

How is heroin addiction treated?

A range of treatments including medicines and behavioral therapies are effective in helping people stop heroin use. It's important to match the best treatment approach to meet the particular needs of each individual patient.

There are medicines being developed to help with the withdrawal process. The FDA approved lofexidine, a non-opioid medicine designed to reduce opioid withdrawal symptoms.

Medicines to help people stop using heroin include buprenorphine and methadone. They work by binding to the same opioid receptors in the brain as heroin, but more weakly, reducing cravings and withdrawal symptoms. Another treatment is naltrexone, which blocks opioid receptors and prevents opioid drugs from having an effect. A NIDA study found that once treatment is initiated, both a buprenorphine/naloxone combination and an extended release naltrexone formulation are similarly effective in addiction. Because full detoxification is necessary for treatment with naloxone, initiating treatment among active users was difficult, but once detoxification was complete, both medications had similar effectiveness.

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[14] . Li W, Li Q, Zhu J, et al. White matter impairment in chronic heroin dependence: a quantitative DTI study. Brain Res. 2013;1531:58-64. doi:10.1016/j.brainres.2013.07.036.

[15] . Liu J, Qin W, Yuan K, et al. Interaction between dysfunctional connectivity at rest and heroin cues-induced brain responses in male abstinent heroin-dependent individuals. PloS One. 2011;6(10):e23098. doi:10.1371/journal.pone.0023098.

[16] . Qiu Y, Jiang G, Su H, et al. Progressive white matter microstructure damage in male chronic heroin dependent individuals: a DTI and TBSS study. PloS One. 2013;8(5):e63212. doi:10.1371/journal.pone.0063212.

Behavioral therapies for heroin addiction include methods called cognitive-behavioral therapy and contingency management. Cognitive-behavioral therapy helps modify the patient's drug-use expectations and behaviors and helps effectively manage triggers and stress. Contingency management provides motivational incentives, such as vouchers or small cash rewards for positive behaviors such as staying drug-free. These behavioral treatment approaches are especially effective when used along with medicines. Read more about drug addiction treatment in our *Treatment Approaches for Drug Addiction DrugFacts.*

Points to Remember

- Heroin is an opioid drug made from morphine, a natural substance taken from the seed pod of various opium poppy plants.
- Heroin can be a white or brown powder, or a black sticky substance known as black tar heroin.
- People inject, sniff, snort, or smoke heroin. Some people mix heroin with crack cocaine, called *speedballing*.
- Heroin enters the brain rapidly and binds to opioid receptors on cells located in many areas, especially those involved in feelings of pain and pleasure and in controlling heart rate, sleeping, and breathing.
- People who use heroin report feeling a "rush" (or euphoria). Other common effects include dry mouth, heavy feelings in the arms and legs, and clouded mental functioning.
- Long-term effects may include collapsed veins, infection of the heart lining and valves, abscesses, and lung complications.
- Research suggests that misuse of prescription opioid pain medicine is a risk factor for starting heroin use.
- A person can overdose on heroin. Naloxone is a medicine that can treat a heroin overdose when given right away, though more than one dose may be needed.
- Heroin can lead to addiction, a form of substance use disorder. Withdrawal symptoms include severe muscle and bone pain, sleep problems, diarrhea and vomiting, and severe heroin cravings.
- A range of treatments including medicines and behavioral therapies are effective in helping people stop heroin use. However, treatment plans should be individualized to meet the needs of the patient.

Learn More

For more information about heroin, visit our:

- Heroin webpage (drugabuse.gov/drugs-abuse/heroin)
- Opioids webpage (drugabuse.gov/drugs-abuse/opioids)

• Commonly Abused Drugs chart

• *Medications to Treat Opioid Addiction Research Report*

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.
Updated June 2019

G. Inhalants

What are inhalants?

Although other substances that are misused can be inhaled, the term *inhalants* refers to the various substances that people typically take *only* by inhaling. These substances include:

- solvents (liquids that become gas at room temperature)
- aerosol sprays
- gases
- nitrites (prescription medicines for chest pain)

Inhalants are various products easily bought and found in the home or workplace—such as spray paints, markers, glues, and cleaning fluids. They contain dangerous substances that have *psychoactive* (mind-altering) properties when inhaled. People don't typically think of these products as drugs because they're not intended for getting "high," but some people use them for that purpose. When these substances are used for getting high, they are called *inhalants*. Inhalants are mostly used by young kids and teens and are the only class of substance used more by younger than by older teens.

How do people use inhalants?

People who use inhalants breathe in the fumes through their nose or mouth, usually by “sniffing,” “snorting,” “bagging,” or “huffing.” It’s called different names depending on the substance and equipment they use.

Although the high that inhalants produce usually lasts just a few minutes, people often try to make it last by continuing to inhale again and again over several hours.

Products Used as Inhalants

Solvents

- industrial or household products, including:
  - paint thinners or removers
  - dry-cleaning fluids
  - gasoline
  - lighter fluid

- art or office supplies, including:
  - correction fluids
  - felt-tip marker fluid
  - electronic contact cleaners
  - glue

Aerosols

- household aerosol items, including:
  - spray paints
  - hair or deodorant sprays
  - aerosol computer cleaning products
  - vegetable oil sprays

Gases

- found in household or commercial products, including:
  - butane lighters
  - propane tanks
  - whipped cream aerosols or dispensers (*whippets*)
  - used as anesthesia (to make patients lose sensation during surgery/procedures), including:
  - ether
  - chloroform
  - nitrous oxide

Nitrites

- often sold in small brown bottles labeled as:
  - video head cleaner
  - room odorizer

- leather cleaner
- liquid aroma

How do inhalants affect the brain?
Most inhalants affect the central nervous system and slow down brain activity. Short-term effects are similar to alcohol and include:

- slurred or distorted speech
- lack of coordination (control of body movement)
- euphoria (feeling "high")
- dizziness

People may also feel light-headed or have *hallucinations* (images/sensations that seem real but aren't) or *delusions* (false beliefs). With repeated inhalations, many people feel less self-conscious and less in control. Some may start vomiting, feel drowsy for several hours, or have a headache that lasts a while.

Unlike other types of inhalants, nitrites, which are often prescribed to treat chest pain, are misused in order to improve sexual pleasure by expanding and relaxing blood vessels.

What are the other health effects of inhalants?
Long-term effects of inhalant use may include:

- liver and kidney damage
- hearing loss
- bone marrow damage
- loss of coordination and limb spasms (from nerve damage)
- delayed behavioral development (from brain problems)
- brain damage (from cut-off oxygen flow to the brain)

In addition, because nitrites are misused for sexual pleasure and performance, they can lead to unsafe sexual practices or other risky behavior. This increases the chance of getting or spreading infectious diseases such as HIV/AIDS or hepatitis.

Read more about drug use and HIV/AIDS in *HIV/AIDS and Drug Abuse: Intertwined Epidemics DrugFacts*.

Can a person overdose on inhalants?

Yes, a person can overdose on inhalants. An overdose occurs when a person uses too much of a drug and has a toxic reaction that results in serious, harmful symptoms or death.

These symptoms can cause seizures and coma. They can even be deadly. Many solvents and aerosol sprays are highly concentrated, meaning they contain a large amount of chemicals with a lot of active ingredients. Sniffing these products can cause the heart to stop within minutes. This condition, known as *sudden sniffing death*, can happen to an otherwise healthy young person the first time he or she uses an inhalant. Using inhalants with a paper or plastic bag or in a closed area may cause death from suffocation (being unable to breathe).

How can an inhalant overdose be treated?
Because inhalant overdose can lead to seizures or cause the heart to stop, first responders and emergency room doctors try to treat the overdose by treating these conditions. They will try to stop the seizure or restart the heart.

Can inhalants cause addiction, a form of substance use disorder?
Although it's not very common, repeated use of inhalants can lead to addiction, a form of substance use disorder (SUD). An SUD develops when continued use of the drug causes issues, such as health problems and failure to meet responsibilities at work, school, or home. An SUD can range from mild to severe, the most severe form being addiction.

Those who try to quit inhalants may have withdrawal symptoms that include:

- nausea
- loss of appetite
- sweating
- problems sleeping
- mood changes

How can people get treatment for addiction to inhalants?
Some people seeking treatment for use of inhalants have found behavioral therapy to be helpful:

- Cognitive-behavioral therapy helps patients recognize, avoid, and cope with the situations in which they are most likely to use drugs.
- Motivational incentives uses vouchers or small cash rewards for positive behaviors such as staying drug-free.

More research is needed to identify the most effective treatment options for addiction to inhalants.

Points to Remember

- Although other substances that are misused can be inhaled, the term *inhalants* refers to the various substances that people typically take *only* by inhaling.
- Inhalants are various products easily bought and found in the home or workplace—such as spray paints, markers, glues, and cleaning fluids. They contain dangerous substances that have *psychoactive* (mind-altering) properties when inhaled.
- People who use inhalants breathe them in through the mouth (*huffing*) or nose.
- Most inhalants affect the central nervous system and slow down brain activity.
- Short-term health effects include slurred or distorted speech, lack of coordination, euphoria (feeling "high"), dizziness, and hallucinations.
- Long-term health effects may include liver and kidney damage, loss of coordination and limb spasms, delayed behavioral development, and brain damage.
- A person can overdose on inhalants. Because inhalant overdose can lead to seizures or cause the heart to stop, first responders and emergency room doctors try to stop the seizure or restart the heart.
- Although it's not very common, repeated use of inhalants can lead to addiction, a form of substance use disorder. Withdrawal symptoms include nausea, sweating, problems sleeping, and mood changes.
- Some people seeking treatment for use of inhalants have found behavioral therapy to be helpful.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.
Updated February 2017

H. Kratom

What is kratom?

Kratom is a tropical tree *(Mitragyna speciosa)* native to Southeast Asia, with leaves that contain compounds that can have psychotropic (mind-altering) effects.

Kratom is not currently an illegal substance and has been easy to order on the internet. It is sometimes sold as a green powder in packets labeled "not for human consumption." It is also sometimes sold as an extract or gum.

Kratom sometimes goes by the following names:

- Biak
- Ketum
- Kakuam
- Ithang
- Thom

How do people use kratom?

Most people take kratom as a pill, capsule, or extract. Some people chew kratom leaves or brew the dried or powdered leaves as a tea. Sometimes the leaves are smoked or eaten in food.

How does kratom affect the brain?

Kratom can cause effects similar to both opioids and stimulants. Two compounds in kratom leaves, *mitragynine* and *7-α-hydroxymitragynine*, interact with opioid receptors in the brain, producing sedation, pleasure, and decreased pain, especially when users consume large amounts of the plant. Mitragynine also interacts with other receptor systems in the brain to produce stimulant effects. When kratom is taken in small amounts, users report increased energy, sociability, and alertness instead of sedation. However, kratom can also cause uncomfortable and sometimes dangerous side effects.

What are the health effects of kratom?

Reported health effects of kratom use include:

- nausea
- itching
- sweating
- dry mouth
- constipation
- increased urination
- loss of appetite
- seizures
- hallucinations

Symptoms of psychosis have been reported in some users.

Can a person overdose on kratom?

There have been multiple reports of deaths in people who had ingested kratom, but most have involved other substances. A 2019 paper analyzing data from the National Poison Data System found that between 2011-2017 there were 11 deaths associated with kratom exposure. Nine of the 11 deaths reported in this study involved kratom plus other drugs and medicines, such as diphenhydramine (an antihistamine), alcohol, caffeine, benzodiazepines, fentanyl, and cocaine. Two deaths were reported following exposure from kratom alone with no other reported substances.* In 2017, the FDA identified at least 44 deaths related to kratom, with at least one case investigated as possible use of pure kratom. The FDA reports note that many of the kratom-associated deaths appeared to have resulted from adulterated products or taking kratom with other potent substances, including illicit drugs, opioids, benzodiazepines, alcohol, gabapentin, and over-the-counter medications, such as cough syrup. Also, there have been some reports of kratom packaged as dietary supplements or dietary ingredients that were laced with other compounds that caused deaths. People should check with their health care providers about the safety of mixing kratom with other medicines.
*(Post et al, 2019. *Clinical Toxicology*).

Is kratom addictive?
Like other drugs with opioid-like effects, kratom might cause dependence, which means users will feel physical withdrawal symptoms when they stop taking the drug. Some users have reported becoming addicted to kratom.

Withdrawal symptoms include:
- muscle aches
- insomnia
- irritability
- hostility
- aggression
- emotional changes
- runny nose
- jerky movements

How is kratom addiction treated?
There are no specific medical treatments for kratom addiction. Some people seeking treatment have found behavioral therapy to be helpful. Scientists need more research to determine how effective this treatment option is.

Does kratom have value as a medicine?

In recent years, some people have used kratom as an herbal alternative to medical treatment in attempts to control withdrawal symptoms and cravings caused by addiction to opioids or to other addictive substances such as alcohol. There is no scientific evidence that kratom is effective or safe for this purpose; further research is needed.

Points to Remember

- Kratom is a tropical tree native to Southeast Asia, with leaves that can have psychotropic effects.
- Kratom is not currently illegal and has been easy to order on the internet.
- Most people take kratom as a pill or capsule. Some people chew kratom leaves or brew the dried or powdered leaves as a tea. Sometimes the leaves are smoked or eaten in food. Two compounds in kratom leaves, mitragynine and *7-α-hydroxymitragynine*, interact with opioid receptors in the brain, producing sedation, pleasure, and decreased pain.
- Mitragynine can also interact with other receptor systems in the brain to produce stimulant effects.
- Reported health effects of kratom use include nausea, sweating, seizures, and psychotic symptoms.
- Commercial forms of kratom are sometimes laced with other compounds that have caused deaths.
- Some users have reported becoming addicted to kratom.
- Behavioral therapies and medications have not specifically been tested for treatment of kratom addiction.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.
Updated September 2018

I. Marijuana

What is marijuana?

Marijuana refers to the dried leaves, flowers, stems, and seeds from the *Cannabis sativa* or *Cannabis indica* plant. The plant contains the mind-altering chemical THC and other similar compounds. Extracts can also be made from the cannabis plant.

Marijuana is the most commonly used psychotropic drug in the United States, after alcohol.[17] Its use is widespread among young people. In 2018, more than 11.8 million young adults used marijuana in the past year.1 According to the Monitoring the Future survey, rates of past year marijuana use among middle and high school students have remained steady, but the number of teens in 8th and 10th grades who say they use it daily has increased. With the growing popularity of vaping devices, teens have started vaping THC (the ingredient in marijuana that produces the high), with nearly 4% of 12th graders saying they vape THC daily. In addition, the number of young people who believe regular marijuana use is risky is decreasing.[18]

Legalization of marijuana for medical use or adult recreational use in a growing number of states may affect these views. Read more about marijuana as medicine in our *DrugFacts: Marijuana as Medicine.*

How do people use marijuana?

People smoke marijuana in hand-rolled cigarettes (*joints*) or in pipes or water pipes (*bongs*). They also smoke it in *blunts*—emptied cigars that have been partly or completely refilled with marijuana. To avoid inhaling smoke, some people are using vaporizers. These devices pull the active ingredients (including THC) from the marijuana and collect their vapor in a storage unit. A person then inhales the vapor, not the smoke. Some vaporizers use a liquid marijuana extract.

People can mix marijuana in food (*edibles*), such as brownies, cookies, or candy, or brew it as a tea. A newly popular method of use is smoking or eating different forms of THC-rich resins.

Marijuana Extracts

Smoking THC-rich resins extracted from the marijuana plant is on the rise. People call this practice *dabbing.* These extracts come in various forms, such as:

- *hash oil* or *honey oil*—a gooey liquid
- *wax* or *budder*—a soft solid with a texture like lip balm
- *shatter*—a hard, amber-colored solid

These extracts can deliver extremely large amounts of THC to the body, and their use has sent some people to the emergency room. Another danger is in preparing these extracts,

[17] Substance Abuse Center for Behavioral Health Statistics and Quality. Results from the 2018 National Survey on Drug Use and Health: Detailed Tables. SAMHSA. https://www.samhsa.gov/data/report/2018-nsduh-detailed-tables Accessed December 2019.

[18] Johnston L, O'Malley P, Miech R, Bachman J, Schulenberg J. *Monitoring the Future National Survey Results on Drug Use: 1975-2015: Overview: Key Findings on Adolescent Drug Use.* Ann Arbor, MI: Institute for Social Research, The University of Michigan; 2015.

which usually involves butane (lighter fluid). A number of people have caused fires and explosions and have been seriously burned from using butane to make extracts at home.[19] [20]

How does marijuana affect the brain?

Marijuana has both short-and long-term effects on the brain.

Short-Term Effects

When a person smokes marijuana, THC quickly passes from the lungs into the bloodstream. The blood carries the chemical to the brain and other organs throughout the body. The body absorbs THC more slowly when the person eats or drinks it. In that case, they generally feel the effects after 30 minutes to 1 hour.

THC acts on specific brain cell receptors that ordinarily react to natural THC-like chemicals. These natural chemicals play a role in normal brain development and function.

Marijuana over activates parts of the brain that contain the highest number of these receptors. This causes the "high" that people feel. Other effects include:

- altered senses (for example, seeing brighter colors)
- altered sense of time
- changes in mood
- impaired body movement
- difficulty with thinking and problem-solving
- impaired memory
- hallucinations (when taken in high doses)
- delusions (when taken in high doses)
- psychosis (risk is highest with regular use of high potency marijuana)

Long-Term Effects

Marijuana also affects brain development. When people begin using marijuana as teenagers, the drug may impair thinking, memory, and learning functions and affect how the brain builds connections between the areas necessary for these functions. Researchers are still studying how long marijuana's effects last and whether some changes may be permanent.

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[19] . Bell C, Slim J, Flaten HK, Lindberg G, Arek W, Monte AA. Butane Hash Oil Burns Associated with Marijuana Liberalization in Colorado. *J Med Toxicol Off J Am Coll Med Toxicol*. 2015;11(4):422-425. doi:10.1007/s13181-015-0501-0

[20] Romanowski KS, Barsun A, Kwan P, et al. Butane Hash Oil Burns: A 7-Year Perspective on a Growing Problem. *J Burn Care Res Off Publ Am Burn Assoc*. 2017;38(1):e165-e171. doi:10.1097/BCR.0000000000000334

For example, a study from New Zealand conducted in part by researchers at Duke University showed that people who started smoking marijuana heavily in their teens and had an ongoing marijuana use disorder lost an average of 8 IQ points between ages 13 and 38. The lost mental abilities didn't fully return in those who quit marijuana as adults. Those who started smoking marijuana as adults didn't show notable IQ declines.[21]

In another recent study on twins, those who used marijuana showed a significant decline in general knowledge and in verbal ability (equivalent to 4 IQ points) between the preteen years and early adulthood, but no predictable difference was found between twins when one used marijuana and the other didn't. This suggests that the IQ decline in marijuana users may be caused by something other than marijuana, such as shared familial factors (e.g., genetics, family environment).[22] NIDA's Adolescent Brain Cognitive Development (ABCD) study, a major longitudinal study, is tracking a large sample of young Americans from late childhood to early adulthood to help clarify how and to what extent marijuana and other substances, alone and in combination, affect adolescent brain development. Read more about the ABCD study on our Longitudinal Study of Adolescent Brain and Cognitive Development (ABCD Study) webpage.

A Rise in Marijuana's THC Levels

The amount of THC in marijuana has been increasing steadily over the past few decades.[23] For a person who's new to marijuana use, this may mean exposure to higher THC levels with a greater chance of a harmful reaction. Higher THC levels may explain the rise in emergency room visits involving marijuana use.

The popularity of edibles also increases the chance of harmful reactions. Edibles take longer to digest and produce a high. Therefore, people may consume more to feel the effects faster, leading to dangerous results.

Higher THC levels may also mean a greater risk for addiction if people are regularly exposing themselves to high doses.

Reports of Deaths Related to Vaping

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[21] . Meier MH, Caspi A, Ambler A, et al. Persistent cannabis users show neuropsychological decline from childhood to midlife. *Proc Natl Acad Sci U S A*. 2012;109(40):E2657-E2664. doi:10.1073/pnas.1206820109

[22] Jackson NJ, Isen JD, Khoddam R, et al. Impact of adolescent marijuana use on intelligence: Results from two longitudinal twin studies. *Proc Natl Acad Sci U S A*. 2016;113(5):E500-E508. doi:10.1073/pnas.1516648113

[23] Mehmedic Z, Chandra S, Slade D, et al. Potency trends of Δ9-THC and other cannabinoids in confiscated cannabis preparations from 1993 to 2008. *J Forensic Sci*. 2010;55(5):1209-1217. doi:10.1111/j.1556-4029.2010.01441.x

The Food and Drug Administration has alerted the public to hundreds of reports of serious lung illnesses associated with vaping, including several deaths. They are working with the Centers for Disease Control and Prevention (CDC) to investigate the cause of these illnesses. Many of the suspect products tested by the states or federal health officials have been identified as vaping products containing THC, the main psychotropic ingredient in marijuana. Some of the patients reported a mixture of THC and nicotine; and some reported vaping nicotine alone. No one substance has been identified in all of the samples tested, and it is unclear if the illnesses are related to one single compound. Until more details are known, FDA officials have warned people not to use any vaping products bought on the street, and they warn against modifying any products purchased in stores. They are also asking people and health professionals to report any adverse effects. The CDC has posted an information page for consumers.

What are the other health effects of marijuana?

Marijuana use may have a wide range of effects, both physical and mental.

Physical Effects

- **Breathing problems.** Marijuana smoke irritates the lungs, and people who smoke marijuana frequently can have the same breathing problems as those who smoke tobacco. These problems include daily cough and phlegm, more frequent lung illness, and a higher risk of lung infections. Researchers so far haven't found a higher risk for lung cancer in people who smoke marijuana.[24]

- **Increased heart rate.** Marijuana raises heart rate for up to 3 hours after smoking. This effect may increase the chance of heart attack. Older people and those with heart problems may be at higher risk.

- **Problems with child development during and after pregnancy.** One study found that about 20% of pregnant women 24-years-old and younger screened positive for marijuana. However, this study also found that women were about twice as likely to screen positive for marijuana use via a drug test than they state in self-reported measures.[25] This suggests that self-reported rates of marijuana use in pregnant females is not an accurate measure of marijuana use and may be underreporting their use. . Additionally, in one study of dispensaries, nonmedical personnel at marijuana

[24] National Academies of Sciences, Engineering, and Medicine. *The Health Effects of Cannabis and Cannabinoids: Current State of Evidence and Recommendations for Research*. Washington, DC: The National Academies Press; 2017.

[25] Young-Wolff KC, Tucker L-Y, Alexeeff S, et al. Trends in Self-reported and Biochemically Tested Marijuana Use Among Pregnant Females in California From 2009-2016. *JAMA*. 2017;318(24):2490. doi:10.1001/jama.2017.17225

dispensaries were recommending marijuana to pregnant women for nausea, but medical experts warn against it. This concerns medical experts because marijuana use during pregnancy is linked to lower birth weight[26] and increased risk of both brain and behavioral problems in babies. If a pregnant woman uses marijuana, the drug may affect certain developing parts of the fetus's brain. Children exposed to marijuana in the womb have an increased risk of problems with attention,[27] memory, and problem-solving compared to unexposed children.[28] Some research also suggests that moderate amounts of THC are excreted into the breast milk of nursing mothers.[29] With regular use, THC can reach amounts in breast milk that could affect the baby's developing brain. Other recent research suggests an increased risk of preterm births. More research is needed. Read our *Marijuana Research Report* for more information about marijuana and pregnancy.

- **Intense nausea and vomiting.** Regular, long-term marijuana use can lead to some people to develop Cannabinoid Hyperemesis Syndrome. This causes users to experience regular cycles of severe nausea, vomiting, and dehydration, sometimes requiring emergency medical attention.[30]

Mental Effects

Long-term marijuana use has been linked to mental illness in some people, such as:

- temporary hallucinations
- temporary paranoia
- worsening symptoms in patients with *schizophrenia*—a severe mental disorder with symptoms such as hallucinations, paranoia, and disorganized thinking

Marijuana use has also been linked to other mental health problems, such as depression, anxiety, and suicidal thoughts among teens. However, study findings have been mixed.

Are there effects of inhaling secondhand marijuana smoke?

Failing a Drug Test?

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[26] The National Academies of Sciences, Engineering, and Medicine, Health and Medicine Division, Board on Population Health and Public Health Practice, Committee on the Health Effects of Marijuana: An Evidence Review and Research Agenda. *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*. http://nationalacademies.org/hmd/Reports/2017/health-effects-of-cannabis-and-cannabinoids.aspx. Accessed January 19, 2017.

[27] Goldschmidt L, Day NL, Richardson GA. Effects of prenatal marijuana exposure on child behavior problems at age 10. *Neurotoxicol Teratol*. 2000;22(3):325-336.

[28] Richardson GA, Ryan C, Willford J, Day NL, Goldschmidt L. Prenatal alcohol and marijuana exposure: effects on neuropsychological outcomes at 10 years. *Neurotoxicol Teratol*. 2002;24(3):309-320.

[29] Perez-Reyes M, Wall ME. Presence of delta9-tetrahydrocannabinol in human milk. *N Engl J Med*. 1982;307(13):819-820. doi:10.1056/NEJM198209233071311

[30] Galli JA, Sawaya RA, Friedenberg FK. Cannabinoid Hyperemesis Syndrome. *Curr Drug Abuse Rev*. 2011;4(4):241-249.

While it's possible to fail a drug test after inhaling secondhand marijuana smoke, it's unlikely. Studies show that very little THC is released in the air when a person exhales. Research findings suggest that, unless people are in an enclosed room, breathing in lots of smoke for hours at close range, they aren't likely to fail a drug test.[31] [32] Even if some THC was found in the blood, it wouldn't be enough to fail a test.

Getting High from Passive Exposure?

Similarly, it's unlikely that secondhand marijuana smoke would give nonsmoking people in a confined space a high from passive exposure. Studies have shown that people who don't use marijuana report only mild effects of the drug from a nearby smoker, under extreme conditions (breathing in lots of marijuana smoke for hours in an enclosed room).[33]

Other Health Effects?

More research is needed to know if secondhand marijuana smoke has similar health risks as secondhand tobacco smoke. A recent study on rats suggests that secondhand marijuana smoke can do as much damage to the heart and blood vessels as secondhand tobacco smoke.[34] But researchers haven't fully explored the effect of secondhand marijuana smoke on humans. What they do know is that the toxins and tar found in marijuana smoke could affect vulnerable people, such as children or people with asthma.

Is marijuana a gateway drug?

Use of alcohol, tobacco, and marijuana are likely to come before use of other drugs.[35] [36] Animal studies have shown that early exposure to addictive substances, including THC, may change how the brain responds to other drugs. For example, when rodents are repeatedly exposed to THC when they're young, they later show an enhanced response to other addictive substances—such as morphine or nicotine—in the areas of the brain that control reward, and they're more likely to show addiction-like behaviors.[37] [38]

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[31] Röhrich J, Schimmel I, Zörntlein S, et al. Concentrations of delta9-tetrahydrocannabinol and 11-nor-9-carboxytetrahydrocannabinol in blood and urine after passive exposure to Cannabis smoke in a coffee shop. *J Anal Toxicol*. 2010;34(4):196-203.

[32] Cone EJ, Bigelow GE, Herrmann ES, et al. Non-smoker exposure to secondhand cannabis smoke. I. Urine screening and confirmation results. *J Anal Toxicol*. 2015;39(1):1-12. doi:10.1093/jat/bku116

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Although these findings support the idea of marijuana as a "gateway drug," the majority of people who use marijuana don't go on to use other "harder" drugs. It's also important to note that other factors besides biological mechanisms, such as a person's social environment, are also critical in a person's risk for drug use and addiction.

How Does Marijuana Affect a Person's Life?

Compared to those who don't use marijuana, those who frequently use large amounts report the following:

- lower life satisfaction
- poorer mental health
- poorer physical health
- more relationship problems

People also report less academic and career success. For example, marijuana use is linked to a higher likelihood of dropping out of school.[39] It's also linked to more job absences, accidents, and injuries.[40]

Can a person overdose on marijuana?

An overdose occurs when a person uses enough of the drug to produce life-threatening symptoms or death. There are no reports of teens or adults dying from marijuana alone. However, some people who use marijuana can feel some very uncomfortable side effects, especially when using marijuana products with high THC levels. People have reported symptoms such as anxiety and paranoia, and in rare cases, an extreme psychotic reaction (which can include delusions and hallucinations) that can lead them to seek treatment in an emergency room.

While a psychotic reaction can occur following any method of use, emergency room responders have seen an increasing number of cases involving marijuana edibles. Some people (especially preteens and teens) who know very little about edibles don't realize that it takes longer for the body to feel marijuana's effects when eaten rather than smoked. So they consume more of the edible, trying to get high faster or thinking they haven't taken enough. In addition, some babies and toddlers have been seriously ill after ingesting marijuana or marijuana edibles left around the house.

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Is marijuana addictive?

Marijuana use can lead to the development of a *substance use disorder,* a medical illness in which the person is unable to stop using even though it's causing health and social problems in their life. Severe substance use disorders are also known as addiction. Research suggests that between 9 and 30 percent of those who use marijuana may develop some degree of marijuana use disorder.[41] People who begin using marijuana before age 18 are four to seven times more likely than adults to develop a marijuana use disorder.[42]

Many people who use marijuana long term and are trying to quit report mild withdrawal symptoms that make quitting difficult. These include:

- grouchiness
- sleeplessness
- decreased appetite
- anxiety
- cravings

What treatments are available for marijuana use disorder?

No medications are currently available to treat marijuana use disorder, but behavioral support has been shown to be effective. Examples include therapy and motivational incentives (providing rewards to patients who remain drug-free). Continuing research may lead to new medications that help ease withdrawal symptoms, block the effects of marijuana, and prevent relapse.

Points to Remember

- Marijuana refers to the dried leaves, flowers, stems, and seeds from the *Cannabis sativa* or *Cannabis indica* plant.
- The plant contains the mind-altering chemical THC and other related compounds.
- People use marijuana by smoking, eating, drinking, or inhaling it.
- Smoking and vaping THC-rich extracts from the marijuana plant (a practice called *dabbing*) is on the rise.
- THC overactivates certain brain cell receptors, resulting in effects such as:
    - altered senses
    - changes in mood
    - impaired body movement

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    - difficulty with thinking and problem-solving
    - impaired memory and learning
- Marijuana use can have a wide range of health effects, including:
    - hallucinations and paranoia
    - breathing problems
    - possible harm to a fetus's brain in pregnant women
- The amount of THC in marijuana has been increasing steadily in recent decades, creating more harmful effects in some people.
- It's unlikely that a person will fail a drug test or get high from passive exposure by inhaling secondhand marijuana smoke.
- There aren't any reports of teens and adults dying from using marijuana alone, but marijuana use can cause some very uncomfortable side effects, such as anxiety and paranoia and, in rare cases, extreme psychotic reactions.
- Marijuana use can lead to a substance use disorder, which can develop into an addiction in severe cases.
- No medications are currently available to treat marijuana use disorder, but behavioral support can be effective.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.
Updated December 2019

J. Marijuana as Medicine

What is medical marijuana?

The term *medical marijuana* refers to using the whole, unprocessed marijuana plant or its basic extracts to treat symptoms of illness and other conditions. The U.S. Food and Drug Administration (FDA) has not recognized or approved the marijuana plant as medicine.

However, scientific study of the chemicals in marijuana, called *cannabinoids*, has led to two FDA-approved medications that contain cannabinoid chemicals in pill form. Continued research may lead to more medications.

Because the marijuana plant contains chemicals that may help treat a range of illnesses and symptoms, many people argue that it should be legal for medical purposes. In fact, a growing number of states have legalized marijuana for medical use.

Why isn't the marijuana plant an FDA-approved medicine?

The FDA requires carefully conducted studies (clinical trials) in hundreds to thousands of human subjects to determine the benefits and risks of a possible medication. So far, researchers haven't conducted enough large-scale clinical trials that show that the benefits of the marijuana plant (as opposed to its cannabinoid ingredients) outweigh its risks in patients it's meant to treat.

Medical Marijuana Laws and Prescription Opioid Use Outcomes

A new study underscores the need for additional research on the effect of medical marijuana laws on opioid overdose deaths and cautions against drawing a causal connection between the two. Early research suggested that there may be a relationship between availability of medical marijuana and opioid analgesic overdose mortality. In particular, a NIDA-funded study published in 2014 found that from 1999 to 2010, states with medical cannabis laws experienced slower rates of increase in opioid analgesic overdose death rates compared to states without such laws.[43]

A 2019 analysis, also funded by NIDA, re-examined this relationship using data through 2017. Similar to the findings reported previously, this research team found that opioid overdose mortality rates between 1999-2010 in states allowing medical marijuana use were 21% lower than expected. When the analysis was extended through 2017, however, they found that the trend reversed, such that states with medical cannabis laws experienced an overdose death rate 22.7% higher than expected.[44] The investigators uncovered no evidence that either broader cannabis laws (those allowing recreational use) or more restrictive laws (those only permitting the use of marijuana with low tetrahydrocannabinol concentrations) were associated with changes in opioid overdose mortality rates.

These data, therefore, do not support the interpretation that access to cannabis reduces opioid overdose. Indeed, the authors note that neither study provides evidence of a causal relationship between marijuana access and opioid overdose deaths. Rather, they suggest that the associations are likely due to factors the researchers did not measure, and they caution against drawing conclusions on an individual level from ecological (population-level) data. Research is still needed on the potential medical benefits of cannabis or cannabinoids.

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[43] Bachhuber MA, Saloner B, Cunningham CO, Barry CL. Medical cannabis laws and opioid analgesic overdose mortality in the United States, 1999-2010. JAMA Intern Med. 2014;174(10):1668-1673. doi:10.1001/jamainternmed.2014.4005

[44] Chelsea L. Shover, Corey S. Davis, Sanford C. Gordon, and Keith Humphreys, Association between medical cannabis laws and opioid overdose mortality has reversed over time, PNAS June 25, 2019 116 (26) 12624-12626.

What are cannabinoids?

Cannabinoids are chemicals related to *delta-9-tetrahydrocannabinol* (THC), marijuana's main mind-altering ingredient that makes people "high." The marijuana plant contains more than 100 cannabinoids. Scientists as well as illegal manufacturers have produced many cannabinoids in the lab. Some of these cannabinoids are extremely powerful and have led to serious health effects when misused.

The body also produces its own cannabinoid chemicals. They play a role in regulating pleasure, memory, thinking, concentration, body movement, awareness of time, appetite, pain, and the senses (taste, touch, smell, hearing, and sight).

How might cannabinoids be useful as medicine?

Currently, the two main cannabinoids from the marijuana plant that are of medical interest are THC and CBD.

Are People with Health- and Age-Related Problems More Vulnerable to Marijuana's Risks?

State-approved medicinal use of marijuana is a fairly new practice. For that reason, marijuana's effects on people who are weakened because of age or illness are still relatively unknown. Older people and those suffering from diseases such as cancer or AIDS could be more vulnerable to the drug's harmful effects, but more research is needed.

THC can increase appetite and reduce nausea. THC may also decrease pain, inflammation (swelling and redness), and muscle control problems.

Unlike THC, CBD is a cannabinoid that doesn't make people "high." These drugs aren't popular for recreational use because they aren't intoxicating. It may be useful in reducing pain and inflammation, controlling epileptic seizures, and possibly even treating mental illness and addictions. The FDA approved a CBD-based liquid medication called Epidiolex® for the treatment of two forms of severe childhood epilepsy, Dravet syndrome and Lennox-Gastaut syndrome.

Many researchers, including those funded by the National Institutes of Health (NIH), are continuing to explore the possible uses of THC, CBD, and other cannabinoids for medical treatment.

For instance, recent animal studies have shown that marijuana extracts may help kill certain cancer cells and reduce the size of others. Evidence from one cell culture study with rodents

suggests that purified extracts from whole-plant marijuana can slow the growth of cancer cells from one of the most serious types of brain tumors. Research in mice showed that treatment with purified extracts of THC and CBD, when used with radiation, increased the cancer-killing effects of the radiation.[45]

Scientists are also conducting preclinical and clinical trials with marijuana and its extracts to treat symptoms of illness and other conditions, such as:

- diseases that affect the immune system, including:
  - HIV/AIDS
  - multiple sclerosis (MS), which causes gradual loss of muscle control
- inflammation
- pain
- seizures
- substance use disorders
- mental disorders

Using Medical Marijuana During and After Pregnancy

Some women report using marijuana to treat severe nausea they have during pregnancy. But there's no research that shows that this practice is safe, and doctors generally don't recommend it.

Pregnant women shouldn't use medical marijuana without first checking with their health care provider. Animal studies have shown that moderate amounts of THC given to pregnant or nursing women could have long-lasting effects on the child, including abnormal patterns of social interactions[46] and learning issues[47] [48].

What medications contain cannabinoids?

Two FDA-approved drugs, dronabinol and nabilone, contain THC. They treat nausea caused by chemotherapy and increase appetite in patients with extreme weight loss caused by AIDS. Continued research might lead to more medications.

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The United Kingdom, Canada, and several European countries have approved nabiximols (Sativex®), a mouth spray containing THC and CBD. It treats muscle control problems caused by MS, but it isn't FDA-approved.

Points to Remember

- The term *medical marijuana* refers to treating symptoms of illness and other conditions with the whole, unprocessed marijuana plant or its basic extracts.
- The FDA has not recognized or approved the marijuana plant as medicine.
- However, scientific study of the chemicals in marijuana called *cannabinoids* has led to two FDA-approved medications in pill form, dronabinol and nabilone, used to treat nausea and boost appetite.
- Cannabinoids are chemicals related to *delta-9-tetrahydrocannabinol* (THC), marijuana's main mind-altering ingredient.
- Currently, the two main cannabinoids from the marijuana plant that are of interest for medical treatment are THC and *cannabidiol* (CBD).
- The body also produces its own cannabinoid chemicals.
- Scientists are conducting preclinical and clinical trials with marijuana and its extracts to treat symptoms of illness and other conditions.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.
Updated July 2019

K. MDMA (Ecstasy/Molly)

What is MDMA?

3,4-methylenedioxy-methamphetamine (MDMA) is a synthetic drug that alters mood and perception (awareness of surrounding objects and conditions). It is chemically similar to both stimulants and hallucinogens, producing feelings of increased energy, pleasure, emotional warmth, and distorted sensory and time perception.

MDMA was initially popular in the nightclub scene and at all-night dance parties ("raves"), but the drug now affects a broader range of people who more commonly call the drug Ecstasy or Molly.

How do people use MDMA?

People who use MDMA usually take it as a capsule or tablet, though some swallow it in liquid form or snort the powder. The popular nickname Molly (slang for "molecular") often refers to the supposedly "pure" crystalline powder form of MDMA, usually sold in capsules. However, people who purchase powder or capsules sold as Molly often actually get other drugs such as synthetic cathinones ("bath salts") instead.

Some people take MDMA in combination with other drugs such as alcohol or marijuana.

How does MDMA affect the brain?

MDMA increases the activity of three brain chemicals:

- Dopamine—produces increased energy/activity and acts in the reward system to reinforce behaviors
- Norepinephrine—increases heart rate and blood pressure, which are particularly risky for people with heart and blood vessel problems
- Serotonin—affects mood, appetite, sleep, and other functions. It also triggers hormones that affect sexual arousal and trust. The release of large amounts of serotonin likely causes the emotional closeness, elevated mood, and empathy felt by those who use MDMA.

Other health effects include:

- nausea
- muscle cramping
- involuntary teeth clenching
- blurred vision
- chills
- sweating

MDMA's effects last about 3 to 6 hours, although many of those who use the drug take a second dose as the effects of the first dose begin to fade. Over the course of the week following moderate use of the drug, a person may experience:

- irritability
- impulsiveness and aggression
- depression
- sleep problems
- anxiety
- memory and attention problems

- decreased appetite
- decreased interest in and pleasure from sex

It's possible that some of these effects may be due to the combined use of MDMA with other drugs, especially marijuana.

What are other health effects of MDMA?
High doses of MDMA can affect the body's ability to regulate temperature. This can lead to a spike in body temperature that can occasionally result in liver, kidney, or heart failure or even death.

In addition, because MDMA can promote trust and closeness, its use—especially combined with sildenafil (Viagra®)—may encourage unsafe sexual behavior. This increases people's risk of contracting or transmitting HIV/AIDS or hepatitis.

Read more about drug use and hepatitis at drugabuse.gov/related-topics/viral-hepatitis-very-real-consequence-substance-use.

Is MDMA addictive?
Research results vary on whether MDMA is addictive. Experiments have shown that animals will self-administer MDMA—an important indicator of a drug's abuse potential—although to a lesser degree than some other drugs such as cocaine.

Some people report signs of addiction, including the following withdrawal symptoms:
- fatigue
- loss of appetite
- depression
- trouble concentrating

Added Risk of MDMA
Adding to MDMA's risks is that pills, capsules, or powders sold as Ecstasy and supposedly "pure" Molly may contain other drugs instead of or in addition to MDMA. Much of the Molly seized by the police contains additives such as cocaine, ketamine, methamphetamine, over-the-counter cough medicine, or synthetic cathinones ("bath salts"). These substances may be extremely dangerous if the person does not know what he or she is taking. They may also be dangerous when combined with MDMA. People who purposely or unknowingly combine such a mixture with other substances, such as marijuana and alcohol, may be putting themselves at even higher risk for harmful health effects.

Does MDMA Have Value in Therapy?

MDMA was first used in the 1970s as an aid in psychotherapy (mental disorder treatment using "talk therapy"). The drug didn't have the support of clinical trials (studies using humans) or approval from the U.S. Food and Drug Administration. In 1985, The U.S. Drug Enforcement Administration labeled MDMA as an illegal drug with no recognized medicinal use. Some researchers remain interested in its value in psychotherapy when given to patients under carefully controlled conditions. MDMA is currently in clinical trials as a possible treatment aid for post-traumatic stress disorder and anxiety in terminally ill patients, and for social anxiety in autistic adults.

How can people get treatment for addiction to MDMA?

There are no specific medical treatments for MDMA addiction. Some people seeking treatment for MDMA addiction have found behavioral therapy to be helpful. Scientists need more research to determine how effective this treatment option is for addiction to MDMA.

Points to Remember

- *3,4-methylenedioxy-methamphetamine* (MDMA) is a synthetic drug that alters mood and perception. It is chemically similar to stimulants and hallucinogens.
- MDMA is commonly called Ecstasy or Molly.
- People who use MDMA typically take it as a capsule or tablet. Many people take it in combination with other drugs.
- MDMA acts by increasing the activity of three brain chemicals: dopamine, norepinephrine, and serotonin.
- Effects include increased energy, distorted perception, involuntary teeth clenching, dangerously high body temperature, and depression.
- Many people are unaware that Ecstasy and supposedly "pure" Molly also often contain not only pure MDMA but other drugs that may be particularly dangerous when mixed with MDMA.
- Research results vary on whether MDMA is addictive. Some people report signs of addiction.
- Some people seeking treatment for MDMA addiction have found behavioral therapy to be helpful. There are no specific medical treatments for MDMA addiction.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.
Updated June 2018

L. Methamphetamine

What is methamphetamine?

Methamphetamine is a powerful, highly addictive stimulant that affects the central nervous system. Crystal methamphetamine is a form of the drug that looks like glass fragments or shiny, bluish-white rocks. It is chemically similar to amphetamine, a drug used to treat attention-deficit hyperactivity disorder (ADHD) and narcolepsy, a sleep disorder.

Other common names for methamphetamine include *blue, crystal, ice, meth,* and *speed*.

How do people use methamphetamine?

People can take methamphetamine by:

- smoking
- swallowing (pill)
- snorting
- injecting the powder that has been dissolved in water/alcohol

Because the "high" from the drug both starts and fades quickly, people often take repeated doses in a "binge and crash" pattern. In some cases, people take methamphetamine in a form of binging known as a "run," giving up food and sleep while continuing to take the drug every few hours for up to several days.

How does methamphetamine affect the brain?

Methamphetamine increases the amount of the natural chemical dopamine in the brain. Dopamine is involved in body movement, motivation, and reinforcement of rewarding behaviors. The drug's ability to rapidly release high levels of dopamine in reward areas of the brain strongly reinforces drug-taking behavior, making the user want to repeat the experience.

Short-Term Effects

Taking even small amounts of methamphetamine can result in many of the same health effects as those of other stimulants, such as cocaine or amphetamines. These include:

- increased wakefulness and physical activity
- decreased appetite
- faster breathing
- rapid and/or irregular heartbeat
- increased blood pressure and body temperature

How Do Manufacturers Make Methamphetamine?

Currently, most methamphetamine in the United States is produced by transactional criminal organizations (TCOs) in Mexico. This methamphetamine is highly pure, potent, and low in price. The drug can be easily made in small clandestine laboratories, with relatively inexpensive over-the-counter ingredients such as pseudoephedrine, a common ingredient in cold medications. To curb this kind of production, the law requires pharmacies and other retail stores to keep a purchase record of products containing pseudoephedrine, and take steps to limit sales.

Methamphetamine production also involves a number of other very dangerous chemicals. Toxic effects from these chemicals can remain in the environment long after the lab has been shut down, causing a wide range of health problems for people living in the area. These chemicals can also result in deadly lab explosions and house fires.

What are other health effects of methamphetamine?

Long-Term Effects

People who inject methamphetamine are at increased risk of contracting infectious diseases such as HIV and hepatitis B and C. These diseases are transmitted through contact with blood or other bodily fluids that can remain on drug equipment. Methamphetamine use can also alter judgment and decision-making leading to risky behaviors, such as unprotected sex, which also increases risk for infection.

Methamphetamine use may worsen the progression of HIV/AIDS and its consequences. Studies indicate that HIV causes more injury to nerve cells and more cognitive problems in people who use methamphetamine than it does in people who have HIV and don't use the drug.1 Cognitive problems are those involved with thinking, understanding, learning, and remembering.

Long-term methamphetamine use has many other negative consequences, including:

- extreme weight loss
- addiction
- severe dental problems ("meth mouth")
- intense itching, leading to skin sores from scratching
- anxiety
- changes in brain structure and function
- confusion
- memory loss

- sleeping problems
- violent behavior
- *paranoia*—extreme and unreasonable distrust of others
- *hallucinations*—sensations and images that seem real though they aren't

In addition, continued methamphetamine use causes changes in the brain's dopamine system that are associated with reduced coordination and impaired verbal learning. In studies of people who used methamphetamine over the long term, severe changes also affected areas of the brain involved with emotion and memory.[49] This may explain many of the emotional and cognitive problems seen in those who use methamphetamine.

Although some of these brain changes may reverse after being off the drug for a year or more, other changes may not recover even after a long period of time.[50] A recent study even suggests that people who once used methamphetamine have an increased the risk of developing Parkinson's disease, a disorder of the nerves that affects movement.

Are there health effects from exposure to secondhand methamphetamine smoke?
Researchers don't yet know whether people breathing in secondhand methamphetamine smoke can get high or have other health effects. What they do know is that people can test positive for methamphetamine after exposure to secondhand smoke.[51] [52] More research is needed in this area.

Can a person overdose on methamphetamine?
Yes, a person can overdose on methamphetamine. An overdose occurs when the person uses too much of a drug and has a toxic reaction that results in serious, harmful symptoms or death.

In 2017, about 15 percent of all drug overdose deaths involved the methamphetamine category, and 50 percent of those deaths also involved an opioid, with half of those cases related to the synthetic opioid fentanyl. (CDC Wonder Multiple Causes of Death—see #42 on

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Meth RR.) It is important to note that cheap, dangerous synthetic opioids are sometimes added to street methamphetamine without the user knowing.

How can a methamphetamine overdose be treated?

Because methamphetamine overdose often leads to a stroke, heart attack, or organ problems, first responders and emergency room doctors try to treat the overdose by treating these conditions, with the intent of:

- restoring blood flow to the affected part of the brain (stroke)
- restoring blood flow to the heart (heart attack)
- treating the organ problems

Is methamphetamine addictive?

Yes, methamphetamine is highly addictive. When people stop taking it, withdrawal symptoms can include:

- anxiety
- fatigue
- severe depression
- psychosis
- intense drug cravings

How is methamphetamine addiction treated?

While research is underway, there are currently no government-approved medications to treat methamphetamine addiction. The good news is that methamphetamine misuse can be prevented and addiction to the drug can be treated with behavioral therapies. The most effective treatments for methamphetamine addiction so far are behavioral therapies, such as:

- cognitive-behavioral therapy, which helps patients recognize, avoid, and cope with the situations likely to trigger drug use.
- motivational incentives, which uses vouchers or small cash rewards to encourage patients to remain drug-free

Research also continues toward development of medicines and other new treatments for methamphetamine use, including vaccines, and noninvasive stimulation of the brain using magnetic fields. People can and do recover from methamphetamine addiction if they have ready access to effective treatments that address the multitude of medical and personal problems resulting from long-term use.

Points to Remember

- Methamphetamine is usually a white, bitter-tasting powder or a pill. Crystal methamphetamine looks like glass fragments or shiny, bluish-white rocks.
- Methamphetamine is a stimulant drug that is chemically similar to amphetamine (a drug used to treat ADHD and narcolepsy).
- People can take methamphetamine by smoking, swallowing, snorting, or injecting the drug.
- Methamphetamine increases the amount of dopamine in the brain, which is involved in movement, motivation, and reinforcement of rewarding behaviors.
- Short-term health effects include increased wakefulness and physical activity, decreased appetite, and increased blood pressure and body temperature.
- Long-term health effects include risk of addiction; risk of contracting HIV and hepatitis; severe dental problems ("meth mouth"); intense itching, leading to skin sores from scratching; violent behavior; and paranoia.
- Methamphetamine can be highly addictive. When people stop taking it, withdrawal symptoms can include anxiety, fatigue, severe depression, psychosis, and intense drug cravings.
- Researchers don't yet know if people breathing in secondhand methamphetamine smoke can get high or suffer other health effects.
- A person can overdose on methamphetamine. Because methamphetamine overdose often leads to a stroke, heart attack, or organ problems, first responders and emergency room doctors try to treat the overdose by treating these conditions.
- The most effective treatments for methamphetamine addiction so far are behavioral therapies. There are currently no government-approved medications to treat methamphetamine addiction.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.
Updated May 2019

M. Over-the-counter medicines

What are over-the-counter (OTC) medicines?

Over-the-counter (OTC) medicines are those that can be sold directly to people without a prescription. OTC medicines treat a variety of illnesses and their symptoms including pain, coughs and colds, diarrhea, constipation, acne, and others. Some OTC medicines have active ingredients with the potential for misuse at higher-than-recommended dosages.

How do people use and misuse OTC medicines?

Misuse of an OTC medicine means:

- taking medicine in a way or dose other than directed on the package
- taking medicine for the effect it causes— for example, to get high
- mixing OTC medicines together to create new products

What are some of the commonly misused OTC medicines?

There are two OTC medicines that are most commonly misused.

Dextromethorphan (DXM) is a cough suppressant found in many OTC cold medicines. The most common sources of abused DXM are "extra-strength" cough syrup, tablets and gel capsules. OTC medications that contain DXM often also contain antihistamines and decongestants. DXM may be swallowed in its original form or may be mixed with soda for flavor, called "robo-tripping" or "skittling." Users sometimes inject it. These medicines are often misused in combination with other drugs, such as alcohol and marijuana.

Loperamide is an anti-diarrheal that is available in tablet, capsule, or liquid form. When misusing loperamide, people swallow large quantities of the medicine. It is unclear how often this drug is misused.

How do these OTC medicines affect the brain?

DXM is an opioid without effects on pain reduction and does not act on the opioid receptors. When taken in large doses, DXM causes a depressant effect and sometimes a hallucinogenic effect, similar to PCP and ketamine. Repeatedly seeking to experience that feeling can lead to addiction—a chronic relapsing brain condition characterized by inability to stop using a drug despite damaging consequences to a person's life and health.

Loperamide is an opioid designed not to enter the brain. However, when taken in large amounts and combined with other substances, it may cause the drug to act in a similar way to other opioids. Other opioids, such as certain prescription pain relievers and heroin, bind to and activate opioid receptors in many areas of the brain, especially those involved in feelings of pain and pleasure. Opioid receptors are also located in the brain stem, which controls important processes, such as blood pressure, arousal, and breathing.

"Behind-the-Counter"

Pseudoephedrine, a nasal decongestant found in many OTC cold medicines, can be used to make methamphetamine. For this reason, products containing pseudoephedrine are sold

“behind the counter” nationwide. A prescription is not needed in most states, but in states that do require a prescription, there are limits on how much a person can buy each month. In some states, only people 18 years of age or older can buy pseudoephedrine.

What are the health effects of these OTC medicines?

DXM

Short-term effects of DXM misuse can range from mild stimulation to alcohol- or marijuana-like intoxication. At high doses, a person may have hallucinations or feelings of physical distortion, extreme panic, paranoia, anxiety, and aggression.

Other health effects from DXM misuse can include the following:

- hyperexcitability
- poor motor control
- lack of energy
- stomach pain
- vision changes
- slurred speech
- increased blood pressure
- sweating

Misuse of DXM products containing acetaminophen can cause liver damage.

Loperamide

In the short-term, loperamide is sometimes misused to lessen cravings and withdrawal symptoms; however, it can cause euphoria, similar to other opioids.

Loperamide misuse can also lead to fainting, stomach pain, constipation, eye changes, and loss of consciousness. It can cause the heart to beat erratically or rapidly, or cause kidney problems. These effects may increase if taken with other medicines that interact with loperamide. Other effects have not been well studied and reports are mixed, but the physical consequences of loperamide misuse can be severe.

Opioid Withdrawal Symptoms

These symptoms include:

- muscle and bone pain
- sleep problems
- diarrhea and vomiting

- cold flashes with goose bumps
- uncontrollable leg movements
- severe cravings

Can a person overdose on these OTC medicines?

Yes, a person can overdose on cold medicines containing DXM or loperamide. An overdose occurs when a person uses enough of the drug to produce a life-threatening reaction or death (Read more on our Intentional vs. Unintentional Overdose Deaths webpage).

As with other opioids, when people overdose on DXM or loperamide, their breathing often slows or stops. This can decrease the amount of oxygen that reaches the brain, a condition called hypoxia. Hypoxia can have short- and long-term mental effects and effects on the nervous system, including coma and permanent brain damage and death.

How can these OTC medicine overdoses be treated?

A person who has overdosed needs immediate medical attention. Call 911. If the person has stopped breathing or if breathing is weak, begin CPR. DXM overdoses can also be treated with naloxone. Read more about naloxone at our Naloxone webpage.

Certain medications can be used to treat heart rhythm problems caused by loperamide overdose. If the heart stops, health care providers will perform CPR and other cardiac support therapies.

Can misuse of these OTC medicines lead to addiction?

Yes, misuse of DXM or loperamide can lead to addiction. An addiction develops when continued use of the drug causes issues, such as health problems and failure to meet responsibilities at work, school, or home.

The symptoms of withdrawal from DXM and loperamide have not been well studied.

How can people get treatment for addiction to these OTC medicines?

There are no medications approved specifically to treat DXM or loperamide addiction. Behavioral therapies, such as cognitive-behavioral therapy and contingency management, may be helpful. Cognitive-behavioral therapy helps modify the patient's drug-use expectations and behaviors, and effectively manage triggers and stress. Contingency management provides vouchers or small cash rewards for positive behaviors such as staying drug-free.

Points to Remember

Over-the-counter (OTC) medicines are those that can be sold directly to people without a prescription. Those that have the potential for misuse include:

- Dextromethorphan (DXM), a cough suppressant found in many OTC cold medicines
- Loperamide, an anti-diarrheal
- When misusing DXM, people swallow large quantities of the medicine, sometimes mixing it with soda for flavor, called "robo-tripping" or "skittling." Loperamide may also be swallowed.
- Short-term effects of DXM misuse can range from mild stimulation to alcohol-or marijuana-like intoxication. Loperamide misuse can cause euphoria, similar to other opioids, or lessen cravings and withdrawal symptoms, but other effects have not been well studied and reports are mixed.
- A person can overdose on cold medicines containing DXM or loperamide.
- Overdose can be treated with CPR and certain medications depending on the person's symptoms, but the most important step to take is to call 911.
- Misuse of DXM or loperamide can lead to addiction.
- There are no medications to treat DXM or loperamide addiction. Behavioral therapies, such as cognitive-behavioral therapy and contingency management, may be helpful.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.
Updated December 2017

N. Prescription CNS Depressants

What are prescription CNS depressants?

Central Nervous System (CNS) depressants are medicines that include sedatives, tranquilizers, and hypnotics. Sedatives primarily include barbiturates (e.g., phenobarbitol) but also include non-benzodiazepine sedative hypnotics such as Ambien® and Lunesta®. Tranquilizers primarily include benzodiazepines, such as Valium® and Xanax®, but also include muscle relaxants and other anti-anxiety medications. These drugs can slow brain activity, making them useful for treating anxiety, panic, acute stress reactions, and sleep disorders.

Some examples of CNS depressants grouped by their respective drug class are:

Benzodiazepines	Non-Benzodiazepine Sedative Hypnotics	Barbiturates
• diazepam (Valium®) • clonazepam (Klonopin®) • alprazolam (Xanax®) • triazolam (Halcion®) • estazolam (Prosom®)	• zolpidem (Ambien®) • eszopiclone (Lunesta®) • zaleplon (Sonata®)	• mephobarbital (Mebaral®) • phenobarbital (Luminal®) • pentobarbital sodium (Nembutal®)

How do people use and misuse prescription CNS depressants?

Most prescription CNS depressants come in pill, capsule, or liquid form, which a person takes by mouth. Misuse of prescription CNS depressants means:

- taking medicine in a way or dose other than prescribed
- taking someone else's medicine
- taking medicine for the effect it causes — to get high

When misusing a prescription CNS depressant, a person can swallow the medicine in its normal form or can crush pills or open capsules.

How do CNS depressants affect the brain?

Most CNS depressants act on the brain by increasing activity of *gamma-aminobutyric acid* (GABA), a chemical that inhibits brain activity. This action causes the drowsy and calming effects that make the medicine effective for anxiety and sleep disorders. People who start taking CNS depressants usually feel sleepy and uncoordinated for the first few days until the body adjusts to these side effects. Other effects from use and misuse can include:

- slurred speech
- poor concentration
- confusion
- headache
- light-headedness
- dizziness
- dry mouth
- problems with movement and memory
- lowered blood pressure

- slowed breathing

If a person takes CNS depressants long term, he or she might need larger doses to achieve therapeutic effects. Continued use can also lead to dependence and withdrawal when use is abruptly reduced or stopped. Suddenly stopping can also lead to harmful consequences like seizures.

Can a person overdose on CNS depressants?
Yes, a person can overdose on CNS depressants. An overdose occurs when the person uses enough of a drug to produce life-threatening symptoms or death (read more on our Intentional vs. Unintentional Overdose Deaths webpage).

When people overdose on a CNS depressant, their breathing often slows or stops. This can decrease the amount of oxygen that reaches the brain, a condition called hypoxia. Hypoxia can have short- and long-term mental effects and effects on the nervous system, including coma and permanent brain damage.

How can a CNS depressant overdose be treated?
The most important step to take is to call 911 so a person who has overdosed can receive immediate medical attention. Flumazenil (Romazicon®) is a medication that medical personnel can use to treat benzodiazepine overdose and has also been shown effective in treating overdose from sleep medicines. The drug might not completely reverse slowed breathing and can lead to seizures in some patients who are taking certain antidepressants. Flumazenil is short acting, and the patient may need more of it every 20 minutes until he or she recovers. For barbiturates and nonbenzodiazepines, body temperature, pulse, breathing, and blood pressure should be monitored while waiting for the drug to be eliminated.

Can prescription CNS depressant use lead to addiction and substance use disorder?
Yes, use or misuse of prescription CNS depressants can lead to problem use, known as a *substance use disorder (SUD),* which takes the form of addiction in severe cases. Long-term use of prescription CNS depressants, even as prescribed by a doctor, can cause some people to develop a tolerance, which means that they need higher and/or more frequent doses of the drug to get the desired effects. A SUD develops when continued use of the drug leads to negative consequences such as health problems or failure to meet responsibilities at work, school, or home, but despite all that the drug use continues.

Those who have become addicted to a prescription CNS depressant and stop using the drug abruptly may experience a withdrawal. Withdrawal symptoms—which can begin as early as a few hours after the drug was last taken—include:

- seizures
- shakiness
- anxiety
- agitation
- insomnia
- overactive reflexes
- increased heart rate, blood pressure, and temperature with sweating
- hallucinations
- severe cravings

People addicted to prescription CNS depressants should not attempt to stop taking them on their own. Withdrawal symptoms from these drugs can be severe and—in the case of certain medications—potentially life-threatening.

How can people get treatment for prescription CNS depressant addiction?

There isn't a lot of research on treating people for addiction to prescription CNS depressants. However, people addicted to these medications should undergo medically supervised detoxification because the dosage they take should be tapered gradually. Counseling, either in an outpatient or inpatient program, can help people through this process. One type of counseling, cognitive-behavioral therapy, focuses on modifying the person's thinking, expectations, and behaviors while improving ways to cope with life's stresses. Cognitive-behavioral therapy has helped people successfully adapt to stop using benzodiazepines.

Often prescription CNS depressant misuse occurs along with the use of other drugs, such as alcohol or opioids. In those cases, the person should seek treatment that addresses the multiple addictions.

Points to Remember

- Prescription CNS depressants are medicines that can slow brain activity to treat anxiety and sleep disorders.
- Prescription CNS depressants act on the brain by increasing activity of GABA, a chemical that slows brain activity.

- People who start taking prescription CNS depressants usually feel sleepy and uncoordinated at first. They can also have poor concentration, confusion, lowered blood pressure, and slowed breathing.
- A person can overdose on prescription CNS depressants. Flumazenil (Romazicon®) can be used to treat benzodiazepine and sleep medicine overdoses. Body temperature, pulse, breathing, and blood pressure should be monitored while waiting for the drug to be eliminated.
- Prescription CNS depressant use or misuse can lead to a substance use disorder, which takes the form of addiction in severe cases, even when used as prescribed by a doctor.
- Withdrawal symptoms include: seizures; shakiness; anxiety; agitation; insomnia; overactive reflexes; increased heart rate, blood pressure, and temperature; hallucinations; and severe cravings.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.

Updated March 2018

N. Prescription Opioids

What are prescription opioids?

Opioids are a class of drugs naturally found in the opium poppy plant. Some prescription opioids are made from the plant directly, and others are made by scientists in labs using the same chemical structure. Opioids are often used as medicines because they contain chemicals that relax the body and can relieve pain. Prescription opioids are used mostly to treat moderate to severe pain, though some opioids can be used to treat coughing and diarrhea. Opioids can also make people feel very relaxed and "high" – which is why they are sometimes used for non-medical reasons. This can be dangerous because opioids can be highly addictive, and overdoses and death are common. Heroin is one of the world's most dangerous opioids, and is never used as a medicine in the United States.

Popular slang terms for opioids include Oxy, Percs, and Vikes.

What are common prescription opioids?

- hydrocodone (Vicodin®) oxycodone (OxyContin®, Percocet®)
- oxymorphone (Opana®)
- morphine (Kadian®, Avinza®)
- codeine
- fentanyl

How do people misuse prescription opioids?

Prescription opioids used for pain relief are generally safe when taken for a short time and as prescribed by a doctor, but they can be misused. People misuse prescription opioids by:

- taking the medicine in a way or dose other than prescribed
- taking someone else's prescription medicine
- taking the medicine for the effect it causes—to get high

When misusing a prescription opioid, a person can swallow the medicine in its normal form. Sometimes people crush pills or open capsules, dissolve the powder in water, and inject the liquid into a vein. Some also snort the powder.

How do prescription opioids affect the brain?

Opioids bind to and activate opioid receptors on cells located in many areas of the brain, spinal cord, and other organs in the body, especially those involved in feelings of pain and pleasure. When opioids attach to these receptors, they block pain signals sent from the brain to the body and release large amounts of dopamine throughout the body. This release can strongly reinforce the act of taking the drug, making the user want to repeat the experience.

What are some possible effects of prescription opioids on the brain and body?

In the short term, opioids can relieve pain and make people feel relaxed and happy. However, opioids can also have harmful effects, including:

- drowsiness
- confusion
- nausea
- constipation
- euphoria
- slowed breathing

Opioid misuse can cause slowed breathing, which can cause hypoxia, a condition that results when too little oxygen reaches the brain. Hypoxia can have short- and long-term psychological and neurological effects, including coma, permanent brain damage, or death. Researchers are also investigating the long-term effects of opioid addiction on the brain, including whether damage can be reversed.

What are the other health effects of opioid medications?

Older adults are at higher risk of accidental misuse or abuse because they typically have multiple prescriptions and chronic diseases, increasing the risk of drug-drug and drug-disease interactions, as well as a slowed metabolism that affects the breakdown of drugs.
Sharing drug injection equipment and having impaired judgment from drug use can increase the risk of contracting infectious diseases such as HIV and from unprotected sex.

Prescription Opioids and Heroin

Prescription opioids and heroin are chemically similar and can produce a similar high. In some places, heroin is cheaper and easier to get than prescription opioids, so some people switch to using heroin instead. Data from 2011 showed that an estimated 4 to 6 percent who misuse prescription opioids switch to heroin1,2,3 and about 80 percent of people who used heroin first misused prescription opioids.1,2,3 More recent data suggest that heroin is frequently the first opioid people use. In a study of those entering treatment for opioid use disorder, approximately one-third reported heroin as the first opioid they used regularly to get high.4

Can I take prescription opioids if I'm pregnant?

If a woman uses prescription opioids when she's pregnant, the baby could develop dependence and have withdrawal symptoms after birth. This is called neonatal abstinence syndrome, which can be treated with medicines. Use during pregnancy can also lead to miscarriage and low birth weight.

It can be difficult for a person with an opioid addiction to quit, but pregnant women who seek treatment have better outcomes than those who quit abruptly. Methadone and buprenorphine are the standard of care to treat opioid-dependent pregnant women. Methadone or buprenorphine maintenance combined with prenatal care and a comprehensive drug treatment program can improve many of the adverse outcomes associated with untreated opioid addiction. If a woman is unable to quit before becoming pregnant, treatment with methadone or buprenorphine during pregnancy improves the chances of having a healthier baby at birth.

In general, it is important to closely monitor women who are trying to quit drug use during pregnancy and to provide treatment as needed.

Can a person overdose on prescription opioids?

Yes, a person can overdose on prescription opioids. An opioid overdose occurs when a person uses enough of the drug to produce life-threatening symptoms or death. When people overdose on an opioid medication, their breathing often slows or stops. This can

decrease the amount of oxygen that reaches the brain, which can result in coma, permanent brain damage, or death.

How can an opioid overdose be treated?

If you suspect someone has overdosed, the most important step to take is to call 911 so he or she can receive immediate medical attention. Once medical personnel arrive, they will administer naloxone. Naloxone is a medicine that can treat an opioid overdose when given right away. It works by rapidly binding to opioid receptors and blocking the effects of opioid drugs. Naloxone is available as an injectable (needle) solution, a hand-held auto-injector (EVZIO®), and a nasal spray (NARCAN® Nasal Spray).

Some states have passed laws that allow pharmacists to dispense naloxone without a personal prescription. This allows friends, family, and others in the community to use the auto-injector and nasal spray versions of naloxone to save someone who is overdosing.

Tolerance vs. Dependence vs. Addiction

Long-term use of prescription opioids, even as prescribed by a doctor, can cause some people to develop **a tolerance**, which means that they need higher and/or more frequent doses of the drug to get the desired effects.

Drug **dependence** occurs with repeated use, causing the neurons to adapt so they only function normally in the presence of the drug. The absence of the drug causes several physiological reactions, ranging from mild in the case of caffeine, to potentially life threatening, such as with heroin. Some chronic pain patients are dependent on opioids and require medical support to stop taking the drug.

Drug **addiction** is a chronic disease characterized by compulsive, or uncontrollable, drug seeking and use despite harmful consequences and long-lasting changes in the brain. The changes can result in harmful behaviors by those who misuse drugs, whether prescription or illicit drugs.

Can use of prescription opioids lead to addiction?

Yes, repeated misuse of prescription opioids can lead to a substance use disorder (SUD), a medical illness which ranges from mild to severe and from temporary to chronic. Addiction is the most severe form of an SUD. An SUD develops when continued misuse of the drug changes the brain and causes health problems and failure to meet responsibilities at work, school, or home.

People addicted to an opioid medication who stop using the drug can have severe withdrawal symptoms that begin as early as a few hours after the drug was last taken. These symptoms include:

- muscle and bone pain
- sleep problems
- diarrhea and vomiting
- cold flashes with goose bumps
- uncontrollable leg movements
- severe cravings

These symptoms can be extremely uncomfortable and are the reason many people find it so difficult to stop using opioids. There are medicines being developed to help with the withdrawal process, and the U.S. Food and Drug Administration (FDA) approved sale of a device, NSS-2 Bridge, that can help ease withdrawal symptoms. The NSS-2 Bridge device is a small electrical nerve stimulator placed behind the person's ear, that can be used for up to five days during the acute withdrawal phase. There are also medicines being developed to help with the withdrawal process. The FDA approved lofexidine, a non-opioid medicine designed to reduce opioid withdrawal symptoms.

What type of treatment can people get for addiction to prescription opioids?

A range of treatments including medicines and behavioral therapies are effective in helping people with opioid addiction.

Two medicines, buprenorphine and methadone, work by binding to the same opioid receptors in the brain as the opioid medicines, reducing cravings and withdrawal symptoms. Another medicine, naltrexone, blocks opioid receptors and prevents opioid drugs from having an effect.

Behavioral therapies for addiction to prescription opioids help people modify their attitudes and behaviors related to drug use, increase healthy life skills, and persist with other forms of treatment, such as medication. Some examples include, cognitive behavioral therapy which helps modify the patient's drug use expectations and behaviors, and also effectively manage triggers and stress. Multidimensional family therapy, developed for adolescents with drug use problems, addresses a range of personal and family influences on one's drug use patterns and is designed to improve overall functioning. These behavioral treatment approaches have proven effective, especially when used along with medicines. Read more about drug addiction treatment in our *Treatment Approaches for Drug Addiction DrugFacts.*

Points to Remember

- Prescription opioids are used mostly to treat moderate to severe pain, though some opioids can be used to treat coughing and diarrhea.
- People misuse prescription opioids by taking the medicine in a way other than prescribed, taking someone else's prescription, or taking the medicine to get high. When misusing a prescription opioid, a person may swallow, inject, or snort the drug.
- Opioids bind to and activate opioid receptors on cells located in the brain, spinal cord, and other organs in the body, especially those involved in feelings of pain and pleasure, and can strongly reinforce the act of taking the drug, making the user want to repeat the experience.
- People who use prescription opioids can feel relaxed and happy, but also experience drowsiness, confusion, nausea, constipation, and slowed breathing.
- Prescription opioids have effects similar to heroin. While prescription opioid misuse is a risk factor for starting heroin use, only a small fraction of people who misuse opioid pain relievers switch to heroin.
- A person can overdose on prescription opioids. Naloxone is a medicine that can treat an opioid overdose when given right away.
- Prescription opioid use, even when used as prescribed by a doctor can lead to a substance use disorder, which takes the form of addiction in severe cases. Withdrawal symptoms include muscle and bone pain, sleep problems, diarrhea and vomiting, and severe cravings.
- A range of treatments including medicines and behavioral therapies are effective in helping people with an opioid use disorder.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.
Updated June 2019

P. Prescription Stimulants

What are prescription stimulants?

Prescription stimulants are medicines generally used to treat attention-deficit hyperactivity disorder (ADHD) and narcolepsy—uncontrollable episodes of deep sleep. They increase alertness, attention, and energy.

What are common prescription stimulants?

• dextroamphetamine (Dexedrine®)
• dextroamphetamine/amphetamine combination product (Adderall®)
• methylphenidate (Ritalin®, Concerta®).

Popular slang terms for prescription stimulants include Speed, Uppers, and Vitamin R.

How do people use and misuse prescription stimulants?

Most prescription stimulants come in tablet, capsule, or liquid form, which a person takes by mouth. Misuse of a prescription stimulant means:

- taking medicine in a way or dose other than prescribed
- taking someone else's medicine
- taking medicine only for the effect it causes—to get high

When misusing a prescription stimulant, people can swallow the medicine in its normal form. Alternatively, they can crush tablets or open the capsules, dissolve the powder in water, and inject the liquid into a vein. Some can also snort or smoke the powder.

Do Prescription Stimulants Make You Smarter?

Some people take prescription stimulants to try to improve mental performance. Teens and college students sometimes misuse them to try to get better grades, and older adults misuse them to try to improve their memory. Taking prescription stimulants for reasons other than treating ADHD or narcolepsy could lead to harmful health effects, such as addiction, heart problems, or psychosis.

How do prescription stimulants affect the brain and body?

Prescription stimulants increase the activity of the brain chemicals *dopamine* and *norepinephrine*. Dopamine is involved in the reinforcement of rewarding behaviors. Norepinephrine affects blood vessels, blood pressure and heart rate, blood sugar, and breathing.

Short-Term Effects

People who use prescription stimulants report feeling a "rush" (euphoria) along with the following:

- increased blood pressure and heart rate
- increased breathing
- decreased blood flow
- increased blood sugar
- opened-up breathing passages

At high doses, prescription stimulants can lead to a dangerously high body temperature, an irregular heartbeat, heart failure, and seizures.

What are the other health effects of prescription stimulants?

Repeated misuse of prescription stimulants, even within a short period, can cause psychosis, anger, or paranoia. If the drug is injected, it is important to note that sharing drug injection equipment and having impaired judgment from drug misuse can increase the risk of contracting infectious diseases such as HIV and hepatitis.

Can a person overdose on prescription stimulants?

Yes, a person can overdose on prescription stimulants. An overdose occurs when the person uses enough of the drug to produce a life-threatening reaction or death.

When people overdose on a prescription stimulant, they most commonly experience several different symptoms, including restlessness, tremors, overactive reflexes, rapid breathing, confusion, aggression, hallucinations, panic states, abnormally increased fever, muscle pains and weakness.

They also may have heart problems, including an irregular heartbeat leading to a heart attack, nerve problems that can lead to a seizure, abnormally high or low blood pressure, and circulation failure. Stomach issues may include nausea, vomiting, diarrhea, and abdominal cramps. In addition, an overdose can result in convulsions, coma, and fatal poisoning.

Risk of Later Substance Use

Some people may be concerned about later substance misuse in children and teens who've been prescribed stimulant drugs to treat ADHD. Studies so far have not shown a difference in later substance use in young people with ADHD treated with prescription stimulants compared with those who didn't receive such treatment. This suggests that treatment with ADHD medication does not positively or negatively affect a person’s risk of developing problem use.

How can a prescription stimulant overdose be treated?

Because prescription stimulant overdose often leads to a heart attack or seizure, the most important step to take is to call 911 so a person who has overdosed can receive immediate medical attention. First responders and emergency room doctors try to treat the overdose with the intent of restoring blood flow to the heart and stopping the seizure with care or with medications if necessary.

Can prescription stimulant use lead to substance use disorder and addiction?

Yes, misuse of prescription stimulants can lead to a *substance use disorder* (SUD), which takes the form of addiction in severe cases. Long-term use of stimulants, even as prescribed by a doctor, can cause a person to develop a tolerance, which means that he or she needs higher and/or more frequent doses of the drug to get the desired effects. An SUD develops when continued use of the drug causes issues, such as health problems and failure to meet responsibilities at work, school, or home. Concerns about use should be discussed with a health care provider.

If a person develops an SUD and stops use of the prescription stimulant, he or she can experience *withdrawal*. Withdrawal symptoms can include:

- fatigue
- depression
- sleep problems

How can people get treatment for prescription stimulant addiction?

Behavioral therapies, including cognitive-behavioral therapy and contingency management (motivational incentives), can be effective in helping to treat people with prescription stimulant addiction. Cognitive-behavioral therapy helps modify the patient's drug-use expectations and behaviors, and it can effectively manage triggers and stress. Contingency management provides vouchers or small cash rewards for positive behaviors such as staying drug-free.

Points to Remember

- Prescription stimulants are medicines used to treat ADHD and narcolepsy.
- Most prescription stimulants come in tablet, capsule, or liquid form, which a person takes by mouth. When misusing a prescription stimulant, a person can swallow, snort, smoke, or inject the drug.
- Prescription stimulants increase the activity of the brain chemicals dopamine and norepinephrine.
- Prescription stimulants increase alertness, attention, and energy. Their misuse, including overdose, can also lead to psychosis, anger, paranoia, heart, nerve, and stomach problems. These issues could lead to a heart attack or seizures.
- Prescription stimulant misuse can lead to a substance use disorder, which takes the form of addiction in severe cases, even when used as prescribed by a doctor. Withdrawal symptoms include fatigue, depression, and sleep problems. Concerns about use should be discussed with a health care provider.
- Behavioral therapies can be effective in helping people stop prescription stimulant misuse, including cognitive-behavioral therapy and contingency management.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.
Updated June 2018

Q. Synthetic Cannabinoids (K2/Spice)

What are synthetic cannabinoids?

Synthetic cannabinoids are human-made mind-altering chemicals that are either sprayed on dried, shredded plant material so they can be smoked or sold as liquids to be vaporized and inhaled in e-cigarettes and other devices. These products are also known as herbal or liquid incense.

These chemicals are called *cannabinoids* because they are similar to chemicals found in the marijuana plant. Because of this similarity, synthetic cannabinoids are sometimes misleadingly called "synthetic marijuana" (or "fake weed"), and they are often marketed as safe, legal alternatives to that drug. In fact, they are not safe and may affect the brain much more powerfully than marijuana; their actual effects can be unpredictable and, in some cases, more dangerous or even life-threatening.

Synthetic cannabinoids are part of a group of drugs called new psychoactive substances (NPS). NPS are unregulated mind-altering substances that have become newly available on the market and are intended to produce the same effects as illegal drugs. Some of these substances may have been around for years but have reentered the market in altered chemical forms, or due to renewed popularity.

False Advertising

Synthetic cannabinoid products are often labeled "not for human consumption." Labels also often claim that they contain "natural" material taken from a variety of plants. However, the only parts of these products that are natural are the dried plant materials. Chemical tests show that the active, mind-altering ingredients are cannabinoid compounds made in laboratories.

Manufacturers sell these products in colorful foil packages and plastic bottles to attract consumers. They market these products under a wide variety of specific brand names. Hundreds of brands now exist, including K2, Spice, Joker, Black Mamba, Kush, and Kronic.

For several years, synthetic cannabinoid mixtures have been easy to buy in drug paraphernalia shops, novelty stores, gas stations, and over the internet. Because the chemicals used in them have no medical benefit and a high potential for abuse, authorities have made it illegal to sell, buy, or possess some of these chemicals. However, manufacturers try to sidestep these laws by changing the chemical formulas in their mixtures.

Easy access and the belief that synthetic cannabinoid products are "natural" and therefore harmless, have likely contributed to their use among young people. Another reason for their continued use is that standard drug tests cannot easily detect many of the chemicals used in these products.

How do people use synthetic cannabinoids?

The most common way to use synthetic cannabinoids is to smoke the dried plant material. Users also mix the sprayed plant material with marijuana or brew it as tea. Other users buy synthetic cannabinoid products as liquids to vaporize in e-cigarettes.

How do synthetic cannabinoids affect the brain?

Synthetic cannabinoids act on the same brain cell receptors as THC (*delta-9-tetrahydrocannabinol)*, the mind-altering ingredient in marijuana.

So far, there have been few scientific studies of the effects of synthetic cannabinoids on the human brain, but researchers do know that some of them bind more strongly than marijuana to the cell receptors affected by THC, and can produce much stronger effects. The resulting health effects can be unpredictable and dangerous.

Because the chemical composition of many synthetic cannabinoid products is unknown and may change from batch to batch, these products are likely to contain substances that cause dramatically different effects than the user might expect.

Synthetic cannabinoid users report some effects similar to those produced by marijuana:

- elevated mood
- relaxation
- altered *perception*—awareness of surrounding objects and conditions
- symptoms of *psychosis*—delusional or disordered thinking detached from reality

Psychotic effects include:

- extreme anxiety
- confusion
- *paranoia*—extreme and unreasonable distrust of others
- *hallucinations*—sensations and images that seem real though they are not

What are some other health effects of synthetic cannabinoids?
People who have used synthetic cannabinoids and have been taken to emergency rooms have shown severe effects including:

- rapid heart rate
- vomiting
- violent behavior
- suicidal thoughts

Synthetic cannabinoids can also raise blood pressure and cause reduced blood supply to the heart, as well as kidney damage and seizures. Use of these drugs is associated with a rising number of deaths.

Are synthetic cannabinoids addictive?
Yes, synthetic cannabinoids can be addictive. Regular users trying to quit may have the following withdrawal symptoms:

- headaches
- anxiety
- depression
- irritability

Behavioral therapies and medications have not specifically been tested for treatment of addiction to these products. Health care providers should screen patients for possible co-occurring mental health conditions.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.
This page was last updated February 2018

R. Synthetic Cathinones (Bath Salts)

What are synthetic cathinones?

Synthetic cathinones, more commonly known as "bath salts," are human-made stimulants chemically related to cathinone, a substance found in the khat plant. Khat is a shrub grown in East Africa and southern Arabia, where some people chew its leaves for their mild stimulant

effects. Human-made versions of cathinone can be much stronger than the natural product and, in some cases, very dangerous.[53]

Synthetic cathinones usually take the form of a white or brown crystal-like powder and are sold in small plastic or foil packages labeled "not for human consumption." They can be labeled as “bath salts,” "plant food," "jewelry cleaner," or "phone screen cleaner."

Synthetic cathinones are part of a group of drugs that concern public health officials called "new psychoactive substances" (NPS). NPS are unregulated psychoactive mind-altering substances with no legitimate medical use and are made to copy the effects of controlled substances. They are introduced and reintroduced into the market in quick succession to dodge or hinder law enforcement efforts to address their manufacture and sale.

Synthetic cathinones are marketed as cheap substitutes for other stimulants such as amphetamines and cocaine. Products sold as Molly often contain synthetic cathinones instead of MDMA (see "Synthetic Cathinones and Molly (Ecstasy)").

People can buy synthetic cathinones online and in drug paraphernalia stores under a variety of brand names, which include:

- Bliss
- Cloud Nine
- Lunar Wave
- Vanilla Sky
- White Lightning

In Name Only

Synthetic cathinone products marketed as "bath salts" should not be confused with products such as Epsom salts that people use during bathing. These bathing products have no mind-altering ingredients.

How do people use synthetic cathinones?

People typically swallow, snort, smoke, or inject synthetic cathinones.

How do synthetic cathinones affect the brain?

[53] Baumann MH. Awash in a sea of “bath salts”: implications for biomedical research and public health. *Addict Abingdon Engl*. 2014;109(10):1577-1579. doi:10.1111/add.12601.

Much is still unknown about how synthetic cathinones affect the human brain. Researchers do know that synthetic cathinones are chemically similar to drugs like amphetamines, cocaine, and MDMA.

A study found that *3,4-methylenedioxypyrovalerone* (MDPV), a common synthetic cathinone, affects the brain in a manner similar to cocaine, but is at least 10 times more powerful. MDPV is the most common synthetic cathinone found in the blood and urine of patients admitted to emergency departments after taking "bath salts."[54]

Synthetic cathinones can produce effects that include:

- paranoia—extreme and unreasonable distrust of others
- hallucinations—experiencing sensations and images that seem real but are not
- increased friendliness
- increased sex drive
- panic attacks
- excited delirium—extreme agitation and violent behavior

Synthetic Cathinones and Molly (Ecstasy)

Molly—slang for "molecular"—refers to drugs that are supposed to be the pure crystal powder form of MDMA.

Usually purchased in capsules, Molly has become more popular in the past few years. Some people use Molly to avoid additives such as caffeine, methamphetamine, and other harmful drugs commonly found in MDMA pills sold as Ecstasy. But those who take what they think is "pure" Molly may be exposing themselves to the same risks.

Law enforcement sources have reported that Molly capsules contain harmful substances including synthetic cathinones. For example, hundreds of Molly capsules tested in two South Florida crime labs in 2012 contained methylone, a dangerous synthetic cathinone.

What are other health effects of synthetic cathinones?

[54] . Baumann MH, Partilla JS, Lehner KR, et al. Powerful Cocaine-Like Actions of 3,4-Methylenedioxypyrovalerone (MDPV), a Principal Constituent of Psychoactive “Bath Salts” Products. *Neuropsychopharmacology*. 2013;38(4):552-562. doi:10.1038/npp.2012.204.

Raised heart rate, blood pressure, and chest pain are some other health effects of synthetic cathinones. People who experience delirium often suffer from dehydration, breakdown of skeletal muscle tissue, and kidney failure.

The worst outcomes are associated with snorting or needle injection. Intoxication from synthetic cathinones has resulted in death.

Are synthetic cathinones addictive?

Yes, synthetic cathinones can be addictive. Animal studies show that rats will compulsively self-administer synthetic cathinones. Human users have reported that the drugs trigger intense, uncontrollable urges to use the drug again. Taking synthetic cathinones can cause strong withdrawal symptoms that include:

- depression
- anxiety
- tremors
- problems sleeping
- paranoia

How can people get treatment for addiction to synthetic cathinones?

Behavioral therapy can be used to treat addiction to synthetic cathinones. Examples include:

- cognitive-behavioral therapy
- contingency management, or motivational incentives—providing rewards to patients who remain substance free
- motivational enhancement therapy
- behavioral treatments geared to teens

As with all addictions, health care providers should screen for co-occurring mental health conditions. While there are no FDA-approved medicines for synthetic cathinone addiction, there are medicines available for common co-occurring conditions.

Points to Remember

- Synthetic cathinones, more commonly known as "bath salts," are drugs that contain one or more human-made chemicals related to cathinone, a stimulant found in the khat plant.
- Synthetic cathinones are marketed as cheap substitutes for other stimulants such as methamphetamine and cocaine. Products sold as Molly (MDMA) can contain synthetic cathinones instead.

- People typically swallow, snort, smoke, or inject synthetic cathinones.
- Much is still unknown about how the chemicals in synthetic cathinones affect the human brain.
- Synthetic cathinones can cause:
    - paranoia
    - increased sociability
    - increased sex drive
    - hallucinations
    - panic attacks
- Intoxication from synthetic cathinones has resulted in death.
- Synthetic cathinones can be addictive.
- Behavioral therapy may be used to treat addiction to synthetic cathinones.
- No medications are currently available to treat addiction to synthetic cathinones.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.
This page was last updated February 2018

S. Vaping Devices (Electronic Cigarettes)

What are vaping devices?

Vaping devices, also known as e-cigarettes, e-vaporizers, or electronic nicotine delivery systems, are battery-operated devices that people use to inhale an aerosol, which typically contains nicotine (though not always), flavorings, and other chemicals. They can resemble traditional tobacco cigarettes (*cig-a-likes)*, cigars, or pipes, or even everyday items like pens or USB memory sticks. Other devices, such as those with fillable tanks, may look different. Regardless of their design and appearance, these devices generally operate in a similar manner and are made of similar components. More than 460 different e-cigarette brands are currently on the market.[55] Some common nicknames for e-cigarettes are:

- e-cigs
- e-hookahs
- hookah pens
- vapes
- vape pens
- mods (customizable, more powerful vaporizers)

[55] . Zhu S-H, Sun JY, Bonnevie E, et al. Four hundred and sixty brands of e-cigarettes and counting: Implications for product regulation. *Tob Control*. 2014;23 Suppl 3:iii3-iii9. doi:10.1136/tobaccocontrol-2014-051670

How do vaping devices work?

Most e-cigarettes consist of four different components, including:

- a cartridge, reservoir or pod, which holds a liquid solution (*e-liquid* or *e-juice*) containing varying amounts of nicotine, flavorings, and other chemicals
- a heating element (atomizer)
- a power source (usually a battery)
- a mouthpiece that the person uses to inhale

In many e-cigarettes, puffing activates the battery-powered heating device, which vaporizes the liquid in the cartridge. The person then inhales the resulting aerosol or vapor (called *vaping*).

Vaping Among Teens

Vaping devices are popular among teens and are now the most commonly used form of nicotine among youth in the United States. Some research shows that many teens do not even realize that vaping cartridges contain nicotine, and assume the pods contain only flavoring. The easy availability of these devices, alluring advertisements, various e-liquid flavors, and the belief that they're safer than cigarettes have helped make them appealing to this age group. In addition, they are easy to hide from teachers and parents because they do not leave behind the stench of tobacco cigarettes and are often disguised as flash drives. Further, a study of high school students found that one in four teens reported using e-cigarettes for *dripping*, a practice in which people produce and inhale vapors by placing e-liquid drops directly onto heated atomizer coils. Teens reported the following reasons for dripping: to create thicker vapor (63.5 percent), to improve flavors (38.7 percent), and to produce a stronger throat hit—a pleasurable feeling that the vapor creates when it causes the throat to contract (27.7 percent).[56] More research is needed on the risks of this practice.

In addition to the unknown health effects, early evidence suggests that vaping might serve as an introductory product for preteens and teens who then go on to use other nicotine products, including cigarettes, which are known to cause disease and premature death. A study showed that students who had used e-cigarettes by the time they started 9th grade were more likely than others to start smoking cigarettes and other smokable tobacco products within the next year.[57] Another study supports these findings, showing that high

[56] Krishnan-Sarin S, Morean M, Kong G, et al. E-Cigarettes and "dripping" among high-school youth. *Pediatrics.* 2017; 139(3). doi: https://doi.org/10.1542/peds.2016-3224

[57] Leventhal AM, Strong DR, Kirkpatrick MG, et al. Association of electronic cigarette use with initiation of combustible tobacco product smoking in early adolescence. *JAMA*. 2015;314(7):700-707. doi:10.1001/jama.2015.8950

school students who used e-cigarettes in the last month were about 7 times more likely to report that they smoked cigarettes when asked approximately six months later, as compared to students who said they didn't use e-cigarettes. Notably, the reverse was not true—students who said they smoked cigarettes were no more likely to report use of e-cigarettes when asked approximately six months later. Like the previous study, these results suggest that teens using e-cigarettes are at a greater risk for smoking cigarettes in the future.[58] Another study has shown an association between e-cigarette smoking and progression to smoking actual cigarettes.[59] This study suggests that vaping nicotine might actually encourage cigarette smoking in adolescents.

Additionally, a study of adult smokers in Europe found those who vaped nicotine were less like to have stopped smoking than those who did not. Those who used e-cigarettes also smoked more cigarettes than those who didn't.[60] In another study of more than 800 people who said they vaped to help them quit traditional cigarette smoking, only nine percent reported having quit when asked a year later.[61] However, more research is still needed to understand if experimenting with e-cigarettes leads to regular use of smokable tobacco. Under U.S. Food and Drug Administration (FDA) regulations designed to protect the health of young Americans, minors can no longer buy e-cigarettes in stores or online (see "Government Regulation of E-cigarettes"). The FDA now regulates the manufacture, import, packaging, labeling, advertising, promotion, sale, and distribution of e-cigarettes. This includes components and parts of e-cigarettes but excludes accessories.

How does vaping affect the brain?

The nicotine in e-liquids is readily absorbed from the lungs into the bloodstream when a person vapes an e-cigarette. Upon entering the blood, nicotine stimulates the adrenal glands to release the hormone epinephrine (adrenaline). Epinephrine stimulates the central nervous system and increases blood pressure, breathing, and heart rate. As with most addictive substances, nicotine activates the brain's reward circuits and also increases levels of a chemical messenger in the brain called *dopamine*, which reinforces rewarding behaviors. Pleasure caused by nicotine's interaction with the reward circuit motivates some people to use nicotine again and again, despite risks to their health and well-being.

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[58] Bold KW, Kong G, Camenga DR, et al. Trajectories of e-cigarette and conventional cigarette use among youth. *Pediatrics*. December 2017:e20171832. doi:10.1542/peds.2017-1832

[59] Chaffee BW, Watkins SL, Glantz SA. Electronic cigarette use and progression from experimentation to established smoking. *Pediatrics*. March 2018:e20173594. doi:10.1542/peds.2017-3594

[60] Kulik MC, Lisha NE, Glantz SA. E-cigarettes associated with depressed smoking cessation: A cross-sectional study of 28 European Union countries. *Am J Prev Med*. 2018;54(4):603-609. doi:10.1016/j.amepre.2017.12.017

[61] . Weaver SR, Huang J, Pechacek TF, Heath JW, Ashley DL, Eriksen MP. Are electronic nicotine delivery systems helping cigarette smokers quit? Evidence from a prospective cohort study of U.S. adult smokers, 2015–2016. *PLOS ONE*. 2018;13(7):e0198047. doi:10.1371/journal.pone.0198047

What are the health effects of vaping? Is it safer than smoking tobacco cigarettes?
Research so far suggests that vaping devices might be less harmful than combustible cigarettes when people who regularly smoke switch to them as a complete replacement. But nicotine in any form is a highly addictive drug. Research suggests it can even prime the brain's reward system, putting vapers at risk for addiction to other drugs.

Also, e-cigarette use exposes the lungs to a variety of chemicals, including those added to e-liquids, and other chemicals produced during the heating/vaporizing process.10 A study of some e-cigarette products found the vapor contains known carcinogens and toxic chemicals, as well as potentially toxic metal nanoparticles from the device itself. The study showed that the e-liquids of certain cig-a-like brands contain high levels of nickel and chromium, which may come from the nichrome heating coils of the vaporizing device. Cig-a-likes may also contain low levels of cadmium, a toxic metal also found in cigarette smoke that can cause breathing problems and disease.11 More research is needed on the health consequences of repeated exposure to these chemicals. There are also reports of lung illnesses and deaths related to inhalation of certain vaping oils into the lungs, which have no way to filter out toxic ingredients.

Reports of Deaths Related to Vaping
The Food and Drug Administration has alerted the public to thousands of reports of serious lung illnesses associated with vaping, including dozens of deaths. They are working with the Centers for Disease Control and Prevention (CDC) to investigate the cause of these illnesses. Many of the suspect products tested by the states or federal health officials have been identified as vaping products containing THC, the main psychotropic ingredient in marijuana. Some of the patients reported a mixture of THC and nicotine; and some reported vaping nicotine alone. While the CDC and FDA continue to investigate possible other contributing substances, CDC has identified a thickening agent—Vitamin E acetate—as a chemical of concern among people with e-cigarette or vaping associated lung injuries. They recommend that people should not use any product containing Vitamin E acetate, or any vaping products containing THC; particularly from informal sources like friends, family, or in-person and online dealers. They also warn against modifying any products purchased in stores, or using any vaping products bought on the street. People, including health professionals, should report any adverse effects of vaping products. The CDC has posted an information page for consumers.

Government Regulation of E-cigarettes

In 2016, the FDA established a rule for e-cigarettes and their liquid solutions. Because e-cigarettes contain nicotine derived from tobacco, they are now subject to government regulation as tobacco products, including the requirement that both in-store and online purchasers be at least 18 years of age (see "E-cigarette Use in Teens").

Health Effects for Teens

The teen years are critical for brain development, which continues into young adulthood. Young people who use nicotine products in any form, including e-cigarettes, are uniquely at risk for long-lasting effects. Because nicotine affects the development of the brain's reward system, continued nicotine vaping can not only lead to nicotine addiction, but it also can make other drugs such as cocaine and methamphetamine more pleasurable to a teen's developing brain.

Nicotine also affects the development of brain circuits that control attention and learning. Other risks include mood disorders and permanent problems with impulse control—failure to fight an urge or impulse that may harm oneself or others.

Can vaping help a person quit smoking?

Some people believe e-cigarettes may help lower nicotine cravings in those who are trying to quit smoking. However, e-cigarettes are not an FDA-approved quit aid, and there is no conclusive scientific evidence on the effectiveness of vaping for long-term smoking cessation. It should be noted that there are seven FDA-approved quit aids that are proven safe and can be effective when used as directed.

Vaping nicotine has not been thoroughly evaluated in scientific studies. For now, not enough data exists on the safety of e-cigarettes, how the health effects compare to traditional cigarettes, and if they are helpful for people trying to quit smoking.

Points to Remember

- People vape with battery-operated devices used to inhale an aerosol, which can contain nicotine, marijuana, flavorings, and other chemicals. In many e-cigarettes, puffing activates the battery-powered heating device, which vaporizes the liquid in the cartridge or reservoir. The person then inhales the resulting aerosol or vapor (called *vaping*).
- Vaping is popular among teens. Under U.S. Food and Drug Administration (FDA) regulations designed to protect the health of young Americans, minors can no longer buy e-cigarettes in stores or online.

- Nicotine stimulates the adrenal glands to release the hormone epinephrine (adrenaline) and increases the levels of a chemical messenger in the brain called *dopamine*. Pleasure caused by nicotine's interaction with the brain's reward system motivates some people to use nicotine again and again, despite possible risks to their health and well-being.
- Research so far suggests that vaping is less harmful than combustible cigarettes when people who regularly smoke switch to them as a complete replacement. But e-cigarettes can still damage a person's health.
- Vaping can lead to nicotine addiction and increased risk for addiction to other drugs.
- Vaping also exposes the lungs to a variety of chemicals, including those added to e-liquids, and other chemicals produced during the heating/vaporizing process.
- More research is needed to determine if vaping nicotine can be as effective as smoking cessation aids already approved by the FDA.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.
Updated December 2019

Chapter 3 – Effects of Drug Use

A. Comorbidity: Substance Use Disorders and Other Mental Illnesses

What is comorbidity?

Comorbidity describes two or more disorders or illnesses occurring in the same person. They can occur at the same time or one after the other. Comorbidity also implies interactions between the illnesses that can worsen the course of both.

Is drug addiction a mental illness?
Yes. Addiction changes the brain in fundamental ways, changing a person's normal needs and desires and replacing them with new priorities connected with seeking and using the drug. This results in compulsive behaviors that weaken the ability to control impulses, despite the negative consequences, and are similar to hallmarks of other mental illnesses.

How common are comorbid substance use disorders and other mental illnesses?
Many people who have a substance use disorder also develop other mental illnesses, just as many people who are diagnosed with mental illness are often diagnosed with a substance

use disorder. For example, about half of people who experience a mental illness will also experience a substance use disorder at some point in their lives and vice versa.[62] [63] Few studies have been done on comorbidity in children, but those that have been conducted suggest that youth with substance use disorders also have high rates of co-occurring mental illness, such as depression and anxiety.

Why do these disorders often co-occur?

Although substance use disorders commonly occur with other mental illnesses, this does not mean that one caused the other, even if one appeared first. In fact, establishing which came first or why can be difficult. However, research suggests three possibilities for this common co-occurrence:

- **Common risk factors can contribute to both mental illness and substance use disorders.** Research suggests that there are many genes that can contribute to the risk of developing both a substance use disorder and a mental illness. For example, some people have a specific gene that can make them at increased risk of mental illness as an adult, if they frequently used marijuana as a child. A gene can also influence how a person responds to a drug – whether or not using the drug makes them feel good. Environmental factors, such as stress or trauma, can cause genetic changes that are passed down through generations and may contribute to the development of mental illnesses or a substance use disorder.
- **Mental illnesses can contribute to drug use and substance use disorders.** Some mental health conditions have been identified as risk factors for developing a substance use disorder.3 For example, some research suggests that people with mental illness may use drugs or alcohol as a form of self-medication.4 Although some drugs may help with mental illness symptoms, sometimes this can also make the symptoms worse. Additionally, when a person develops a mental illness, brain changes may enhance the rewarding effects of substances, predisposing the person to continue using the substance.4
- **Substance use and addiction can contribute to the development of mental illness.** Substance use may change the brain in ways that make a person more likely to develop a mental illness.

How are these comorbid conditions diagnosed and treated?

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[62] . Ross S, Peselow E. Co-occurring psychotic and addictive disorders: neurobiology and diagnosis. *Clin Neuropharmacol*. 2012;35(5):235-243. doi:10.1097/WNF.0b013e318261e193

[63] . Kelly TM, Daley DC. Integrated Treatment of Substance Use and Psychiatric Disorders. *Soc Work Public Health*. 2013;28(0):388-406. doi:10.1080/19371918.2013.774673

The high rate of comorbidity between substance use disorders and other mental illnesses calls for a comprehensive approach that identifies and evaluates both. Accordingly, anyone seeking help for either substance use, misuse, or addiction or another mental disorder should be evaluated for both and treated accordingly.

Several behavioral therapies have shown promise for treating comorbid conditions. These approaches can be tailored to patients according to age, the specific drug misused, and other factors. They can be used alone or in combinations with medications. Some effective behavioral therapies for treating comorbid conditions include:

- Cognitive behavioral therapy (CBT) helps to change harmful beliefs and behaviors.
- Dialectical behavioral therapy (DBT) was designed specifically to reduce self-harm behaviors including suicide attempts, thoughts, or urges; cutting; and drug use.
- Assertive community treatment (ACT) emphasizes outreach to the community and an individualized approach to treatment.
- Therapeutic communities (TC) are a common form of long-term residential treatment that focus on the "resocialization" of the person.
- Contingency management (CM) gives vouchers or rewards to people who practice healthy behaviors.
- Effective medications exist for treating opioid, alcohol, and nicotine addiction and for alleviating the symptoms of many other mental disorders, yet most have not been well studied in comorbid populations. Some medications may benefit multiple problems. For example, bupropion is approved for treating both depression (Wellbutrin®) and nicotine dependence (Zyban®). More research is needed, however, to better understand how these medications work, particularly when combined in patients with comorbidities.

Points to Remember

- Comorbidity describes two or more conditions appearing in a person. The conditions can occur at the same time or one right after the other.
- Comorbid substance use disorder and mental illnesses are common, with about half of people who have one condition also having the other.
- Substance use disorders and mental illnesses have many of the same risk factors. Additionally, having a mental illness may predispose someone to develop a substance use disorder and vice versa.
- Treatment for comorbid illnesses should focus on both mental illness and substance use disorders together, rather than one or the other.

- Effective behavioral treatments and medication exist to treat mental illnesses and addiction.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.
This page was last updated August 2018.

B. Drug Use and Viral Infections (HIV, Hepatitis)

What's the relationship between drug use and viral infections?

People who engage in drug use or high-risk behaviors associated with drug use put themselves at risk for contracting or transmitting viral infections such as human immunodeficiency virus (HIV), acquired immune deficiency syndrome (AIDS), or hepatitis. This is because viruses spread through blood or other body fluids. It happens primarily in two ways: (1) when people inject drugs and share needles or other drug equipment and (2) when drugs impair judgment and people have unprotected sex with an infected partner. This can happen with both men and women.

Drug use and addiction have been inseparably linked with HIV/AIDS since AIDS was first identified as a disease. According to the CDC, one in 10 HIV diagnoses occur among people who inject drugs. In 2016, injection drug use (IDU) contributed to nearly 20 percent of recorded HIV cases among men—more than 150,000 patients. Among females, 21 percent (about 50,000) of HIV cases were attributed to IDU. Additionally, women who become infected with a virus can pass it to their baby during pregnancy, regardless of their drug use. They can also pass HIV to the baby through breastmilk.

What is HIV/AIDS?

HIV stands for *human immunodeficiency virus*. This virus infects the body's immune cells, called CD4 cells (T cells), which are needed to fight infections. HIV lowers the number of these T cells in the immune system, making it harder for the body to fight off infections and disease. *Acquired immune deficiency syndrome* (AIDS), is the final stage of an HIV infection when the body is unable to fend off disease. A person with a healthy immune system has a T cell count between 500 and 1,600.

Being infected with HIV does not automatically mean that it will progress to AIDS. A patient is diagnosed with AIDS when identified with one or more infections and a T cell count of less than 200.

More than 1.1 million people in the United States live with an HIV infection, with an estimated 162,500 who are unaware of their condition. While there are medicines that help prevent the transmission and spread of HIV and its progression to AIDS, there is no vaccine yet developed for the virus, and there is no cure.

What is hepatitis?

Hepatitis is an inflammation of the liver and can cause painful swelling and irritation, most often caused by a family of viruses: A, B, C, D, and E. Each has its own way of spreading to other people and needs its own treatment. Hepatitis B virus (HBV) and hepatitis C virus (HCV) can spread through sharing needles and other drug equipment. Infections can also be transmitted through risky sexual behaviors linked to drug use, though this is not common with HCV.

Hepatitis can lead to cirrhosis—scarring of the liver—resulting in loss of liver function. It can also lead to liver cancer. In fact, HBV and HCV infections are the major risk factors for liver cancer in the United States.

There is a vaccine to prevent HBV infection and medicines to treat it. There are also medicines to treat HCV infection, but no vaccine. Some people recover from infection without treatment. Other people need to take medicine for the rest of their lives and be monitored for liver failure and cancer.

How does drug use affect symptoms and outcomes of a viral infection?

Drug use can worsen the progression of HIV and its symptoms, especially in the brain. Studies show that drugs can make it easier for HIV to enter the brain and cause greater nerve cell injury and problems with thinking, learning, and memory. Drug and alcohol use can also directly damage the liver, increasing risk for chronic liver disease and cancer among those infected with HBV or HCV.

How can people lessen the spread of viral infections?

People can reduce the risk of getting or passing on a viral infection by:

- **Not using drugs.** This decreases the chance of engaging in unsafe behavior, such as sharing drug-use equipment and having unprotected sex, which can lead to these infections.

•**Never sharing drug equipment.** However, if you inject drugs, never share needles or injection equipment. Many communities have syringe services programs (SSPs)where you can get free sterile needles and syringes and safely dispose of used ones. They can also refer you to substance use disorder treatment services and help you get tested for HIV and hepatitis. Contact your local health department or North American Syringe Exchange Network (NASEN)to find an SSP. Also, some pharmacies may sell needles without a prescription. Read more about safe disposal in the U.S. Food and Drug Administration fact sheet, Be Smart With Sharps.

•**Getting tested and treated for viral infection.** People who inject drugs should get tested for HIV, HBV, and HCV. Those who are infected may look and feel fine for years and may not even be aware of the infection. So, testing is needed to help prevent the spread of disease—whether or not you are among those most at risk or part of the general population. Get treatment if needed. Read more about HIV testing at the HIV.gov webpage, HIV Test Types. Read more about hepatitis in the CDC's factsheet, *Hepatitis C: Information on Testing and Diagnosis*.

•**Practicing safe sex every time.** People can reduce their chances of transmitting or getting HIV, HBV, and HCV by using a condom every time they have sex. This is true for those who use drugs and those in the general population.

•**Pre-exposure prophylaxis (PrEP)for HIV**. PrEP is when people who are at significant risk for contracting HIV take a daily dose of HIV medications to prevent them from getting the infection. Research has shown that PrEP has been effective in reducing the risk of HIV infection in people who inject drugs.

•**Post-exposure prophylaxis (PEP)for HIV**. PEP is when people take antiretroviral medicines to prevent becoming infected after being potentially exposed to HIV. According to the CDC, PEP should be used within 72 hours after a recent possible exposure and only be used in emergency situations. If you think you've recently been exposed to HIV during sex, through sharing needles, or sexual assault, talk to your health care provider or an emergency room doctor about PEP right away. Read more about PEP in the Centers for Disease Control and Prevention's (CDC's) factsheet, PEP 101.

•**Getting vaccinated for HBV.** If you live in the same household, have sexual contact with or share needles with a person with HBV, then you should be vaccinated to prevent transmission. Read more about the vaccine on the CDC's webpage, HepatitisB In-short.

•**Getting treatment for substance use disorder.** Talk with a counselor, doctor, or other health care provider about substance use disorder treatment, including medications if you have opioid use disorder.

Points to Remember

- People who engage in drug use or high-risk behaviors associated with drug use put themselves at risk for contracting or transmitting viral infections. This is because viruses spread through blood or other body fluids.
- The viral infections of greatest concern related to drug use are HIV and hepatitis.
- People can get or transmit a viral infection when they inject drugs and share needles or other drug equipment.
- Drugs also impair judgment and can cause people to make risky decisions, including having unprotected sex.
- Women who become infected with a virus can pass it to their baby during pregnancy or while breastfeeding, whether or not they use drugs.
- People can reduce their risk of getting or passing on a viral infection by not using drugs, taking PrEP if they are at high risk for infection, getting PEP if you've been exposed to HIV, getting tested for HIV and HCV, consistently practicing safer sex, getting the HBV vaccine, and getting treatment for drug use.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services. This page was last updated July 2019.

C. Drugged Driving

Drugged driving is driving a vehicle while impaired due to the intoxicating effects of recent drug use. It can make driving a car unsafe—just like driving after drinking alcohol. Drugged driving puts the driver, passengers, and others who share the road at serious risk.

Why is drugged driving dangerous?

The effects of specific drugs on driving skills differ depending on how they act in the brain. For example, marijuana can slow reaction time, impair judgment of time and distance, and decrease coordination. Drivers who have used cocaine or methamphetamine can be aggressive and reckless when driving. Certain kinds of prescription medicines, including benzodiazepines and opioids, can cause drowsiness, dizziness, and impair cognitive functioning (thinking and judgment). All of these effects can lead to vehicle crashes.

Research studies have shown negative effects of marijuana on drivers, including an increase in lane weaving, poor reaction time, and altered attention to the road. Use of alcohol with marijuana makes drivers more impaired, causing even more lane weaving. Some studies report that opioids can cause drowsiness and impair thinking and judgment. Other studies

have found that being under the influence opioids while driving can double your risk of having a crash.

It is difficult to determine how specific drugs affect driving because people tend to mix various substances, including alcohol. But we do know that even small amounts of some drugs can have a measurable effect. As a result, some states have zero-tolerance laws for drugged driving. This means a person can face charges for driving under the influence (DUI) if there is *any* amount of drug in the blood or urine. Many states are waiting to develop laws until research can better define blood levels that indicate impairment, such as those they use with alcohol.

How many people take drugs and drive?

According to the 2017 National Survey on Drug Use and Health (NSDUH), in 2017, 21.4 million people aged 16 or older drove under the influence of alcohol in the past year and 12.8 million drove under the influence of illicit drugs.

The survey also showed that men are more likely than women to drive under the influence of drugs or alcohol. A higher percentage of adults aged 21 to 25 drive after taking drugs or drinking than do young adults aged 16 to 20 or adults 26 or older.

Which drugs are linked to drugged driving?

After alcohol, marijuana is the drug most often found in the blood of drivers involved in crashes. Tests for detecting marijuana in drivers measure the level of *delta-9-tetrahydrocannabinol* (THC), marijuana's mind-altering ingredient, in the blood. But the role that marijuana plays in crashes is often unclear. THC can be detected in body fluids for days or even weeks after use, and it is often combined with alcohol. The vehicle crash risk associated with marijuana in combination with alcohol, cocaine, or benzodiazepines appears to be greater than that for each drug by itself.

Several studies have shown that drivers with THC in their blood were roughly twice as likely to be responsible for a deadly crash or be killed than drivers who hadn't used drugs or alcohol.

However, a large NHTSA study found no significant increased crash risk traceable to marijuana after controlling for drivers' age, gender, race, and presence of alcohol. More research is needed.

Along with marijuana, prescription drugs are also commonly linked to drugged driving crashes. In 2016, 19.7 percent of drivers who drove while under the influence tested positive for some type of opioid.

How often does drugged driving cause crashes?

It's hard to measure how many crashes are caused by drugged driving. This is because:

- a good roadside test for drug levels in the body doesn't yet exist
- some drugs can stay in your system for days or weeks after use, making it difficult to determine when the drug was used, and therefore, how and if it impaired driving
- police don't usually test for drugs if drivers have reached an illegal blood alcohol level because there's already enough evidence for a DUI charge
- many drivers who cause crashes are found to have both drugs and alcohol or more than one drug in their system, making it hard to know which substance had the greater effect

However, according to the Governors Highway Safety Association, 43.6 percent of fatally injured drivers in 2016 tested positive for drugs and over half of those drivers were positive for two or more drugs.

Effects of Commonly Misused Drugs on Driving

Marijuana affects psychomotor skills and cognitive functions critical to driving including vigilance, drowsiness, time and distance perception, reaction time, divided attention, lane tracking, coordination, and balance.
Opioids can cause drowsiness and can impair cognitive function.

Alcohol can reduce coordination, concentration, ability to track moving objects and reduce response to emergency driving situations as well as difficulty steering and maintaining lane position. It can also cause drowsiness.

What populations are especially affected by drugged driving?

Teen and older adult drivers are most often affected by drugged driving. Teens are less experienced and are more likely than other drivers to underestimate or not recognize dangerous situations. They are also more likely to speed and allow less distance between vehicles. When lack of driving experience is combined with drug use, the results can be tragic. Car crashes are the leading cause of death among young people aged 16 to 19 years.

A study of college students with access to a car found that 1 in 6 had driven under the influence of a drug other than alcohol at least once in the past year. Marijuana was the most common drug used, followed by cocaine and prescription pain relievers.

Mental decline in older adults can lead to taking a prescription drug more or less often than they should or in the wrong amount. Older adults also may not break down the drug in their system as quickly as younger people. These factors can lead to unintended intoxication while behind the wheel of a car.

What steps can people take to prevent drugged driving?
Because drugged driving puts people at a higher risk for crashes, public health experts urge people who use drugs and alcohol to develop social strategies to prevent them from getting behind the wheel of a car while impaired. Steps people can take include:

- offering to be a designated driver
- appointing a designated driver to take all car keys
- getting a ride to and from parties where there are alcohol and/or drugs.
- discussing the risks of drugged driving with friends in advance

Points to Remember

- Use of illicit drugs or misuse of prescription drugs can make driving a car unsafe—just like driving after drinking alcohol.
- In 2017, 21.4 million people aged 16 or older drove under the influence of alcohol in the past year and 12.8 million drove under the influence of illicit drugs.
- It's hard to measure how many crashes are caused by drugged driving, but estimates show that almost 44 percent of drivers in fatal car crashes tested positive for drugs.
- Driving under the influence of marijuana, opioids and alcohol can have profound effects on driving.
- People who use drugs and alcohol should develop social strategies to prevent them from getting behind the wheel of a car while impaired.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.
Updated March 2019

D. Understanding Drug Use and Addiction

Many people don't understand why or how other people become addicted to drugs. They may mistakenly think that those who use drugs lack moral principles or willpower and that they could stop their drug use simply by choosing to. In reality, drug addiction is a complex disease, and quitting usually takes more than good intentions or a strong will. Drugs change the brain in ways that make quitting hard, even for those who want to. Fortunately, researchers know more than ever about how drugs affect the brain and have found treatments that can help people recover from drug addiction and lead productive lives.

What is drug addiction?

Addiction is a chronic disease characterized by drug seeking and use that is compulsive, or difficult to control, despite harmful consequences. The initial decision to take drugs is voluntary for most people, but repeated drug use can lead to brain changes that challenge an addicted person's self-control and interfere with their ability to resist intense urges to take drugs. These brain changes can be persistent, which is why drug addiction is considered a "relapsing" disease—people in recovery from drug use disorders are at increased risk for returning to drug use even after years of not taking the drug.

It's common for a person to relapse, but relapse doesn't mean that treatment doesn't work. As with other chronic health conditions, treatment should be ongoing and should be adjusted based on how the patient responds. Treatment plans need to be reviewed often and modified to fit the patient's changing needs.

What happens to the brain when a person takes drugs?

Most drugs affect the brain's "reward circuit," causing euphoria as well as flooding it with the chemical messenger dopamine. A properly functioning reward system motivates a person to repeat behaviors needed to thrive, such as eating and spending time with loved ones. Surges of dopamine in the reward circuit cause the reinforcement of pleasurable but unhealthy behaviors like taking drugs, leading people to repeat the behavior again and again.

As a person continues to use drugs, the brain adapts by reducing the ability of cells in the reward circuit to respond to it. This reduces the high that the person feels compared to the high they felt when first taking the drug—an effect known as tolerance. They might take more of the drug to try and achieve the same high. These brain adaptations often lead to the person becoming less and less able to derive pleasure from other things they once enjoyed, like food, sex, or social activities.

Long-term use also causes changes in other brain chemical systems and circuits as well, affecting functions that include:

- learning
- judgment
- decision-making
- stress
- memory
- behavior

Despite being aware of these harmful outcomes, many people who use drugs continue to take them, which is the nature of addiction.

Why do some people become addicted to drugs while others don't?

No one factor can predict if a person will become addicted to drugs. A combination of factors influences risk for addiction. The more risk factors a person has, the greater the chance that taking drugs can lead to addiction. For example:

• **Biology**. The genes that people are born with account for about half of a person's risk for addiction. Gender, ethnicity, and the presence of other mental disorders may also influence risk for drug use and addiction.

• **Environment**. A person's environment includes many different influences, from family and friends to economic status and general quality of life. Factors such as peer pressure, physical and sexual abuse, early exposure to drugs, stress, and parental guidance can greatly affect a person's likelihood of drug use and addiction.

- **Development**. Genetic and environmental factors interact with critical developmental stages in a person's life to affect addiction risk. Although taking drugs at any age can lead to addiction, the earlier that drug use begins, the more likely it will progress to addiction. This is particularly problematic for teens. Because areas in their brains that control decision-making, judgment, and self-control are still developing, teens may be especially prone to risky behaviors, including trying drugs.

Can drug addiction be cured or prevented?

As with most other chronic diseases, such as diabetes, asthma, or heart disease, treatment for drug addiction generally isn't a cure. However, addiction is treatable and can be successfully managed. People who are recovering from an addiction will be at risk for relapse for years and possibly for their whole lives. Research shows that combining addiction treatment medicines with behavioral therapy ensures the best chance of success for most patients. Treatment approaches tailored to each patient's drug use patterns and any co-occurring medical, mental, and social problems can lead to continued recovery.

More good news is that drug use and addiction are preventable. Results from NIDA-funded research have shown that prevention programs involving families, schools, communities, and the media are effective for preventing or reducing drug use and addiction. Although personal events and cultural factors affect drug use trends, when young people view drug use as harmful, they tend to decrease their drug taking. Therefore, education and outreach are key in helping people understand the possible risks of drug use. Teachers, parents, and health care providers have crucial roles in educating young people and preventing drug use and addiction.

Points to Remember

- Drug addiction is a chronic disease characterized by drug seeking and use that is compulsive, or difficult to control, despite harmful consequences.
- Brain changes that occur over time with drug use challenge an addicted person's self-control and interfere with their ability to resist intense urges to take drugs. This is why drug addiction is also a relapsing disease.
- Relapse is the return to drug use after an attempt to stop. Relapse indicates the need for more or different treatment.
- Most drugs affect the brain's reward circuit by flooding it with the chemical messenger dopamine. Surges of dopamine in the reward circuit cause the reinforcement of pleasurable but unhealthy activities, leading people to repeat the behavior again and again.
- Over time, the brain adjusts to the excess dopamine, which reduces the high that the person feels compared to the high they felt when first taking the drug—an effect known as tolerance. They might take more of the drug, trying to achieve the same dopamine high.
- No single factor can predict whether a person will become addicted to drugs. A combination of genetic, environmental, and developmental factors influences risk for addiction. The more risk factors a person has, the greater the chance that taking drugs can lead to addiction.
- Drug addiction is treatable and can be successfully managed.
- More good news is that drug use and addiction are preventable. Teachers, parents, and health care providers have crucial roles in educating young people and preventing drug use and addiction.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.
Updated June 2018

Chapter 4 – Prevention and Treatment

A. Lessons from Prevention Research

The principles listed below are the result of long-term research studies on the origins of drug abuse behaviors and the common elements of effective prevention programs. These principles were developed to help prevention practitioners use the results of prevention research to address drug use among children, adolescents, and young adults in communities across the country. Parents, educators, and community leaders can use these principles to help guide their thinking, planning, selection, and delivery of drug abuse prevention programs at the community level.

Prevention programs are generally designed for use in a particular setting, such as at home, at school, or within the community, but can be adapted for use in several settings. In addition, programs are also designed with the intended audience in mind: for everyone in the population, for those at greater risk, and for those already involved with drugs or other problem behaviors. Some programs can be geared for more than one audience.

NIDA's prevention research program focuses on risks for drug abuse and other problem behaviors that occur throughout a child's development, from pregnancy through young adulthood. Research funded by NIDA and other Federal research organizations—such as the National Institute of Mental Health and the Centers for Disease Control and Prevention—shows that early intervention can prevent many adolescent risk behaviors.

Principle 1 - Prevention programs should enhance protective factors and reverse or reduce risk factors (Hawkins et al. 2002).

- The risk of becoming a drug abuser involves the relationship among the number and type of risk factors (e.g., deviant attitudes and behaviors) and protective factors (e.g., parental support) (Wills et al. 1996).

- The potential impact of specific risk and protective factors changes with age. For example, risk factors within the family have greater impact on a younger child, while association with drug-abusing peers may be a more significant risk factor for an adolescent (Gerstein and Green 1993; Dishion et al. 1999).

- Early intervention with risk factors (e.g., aggressive behavior and poor self-control) often has a greater impact than later intervention by changing a child's life path (trajectory) away from problems and toward positive behaviors (Ialongo et al. 2001; Hawkins et al. 2008).

- While risk and protective factors can affect people of all groups, these factors can have a different effect depending on a person's age, gender, ethnicity, culture, and environment (Beauvais et al. 1996; Moon et al. 1999).

Principle 2 - Prevention programs should address all forms of drug abuse, alone or in combination, including the underage use of legal drugs (e.g., tobacco or alcohol); the use of illegal drugs (e.g., marijuana or heroin); and the inappropriate use of legally obtained substances (e.g., inhalants), prescription medications, or over-the-counter drugs (Johnston et al. 2002).

Principle 3 - Prevention programs should address the type of drug abuse problem in the local community, target modifiable risk factors, and strengthen identified protective factors (Hawkins et al. 2002).

Principle 4 - Prevention programs should be tailored to address risks specific to population or audience characteristics, such as age, gender, and ethnicity, to improve program effectiveness (Oetting et al. 1997; Olds et al. 1998; Fisher et al. 2007; Brody et al. 2008).

Principle 5 - Family-based prevention programs should enhance family bonding and relationships and include parenting skills; practice in developing, discussing, and enforcing family policies on substance abuse; and training in drug education and information (Ashery et al. 1998).

Family bonding is the bedrock of the relationship between parents and children. Bonding can be strengthened through skills training on parent supportiveness of children, parent-child communication, and parental involvement (Kosterman et al. 1997; Spoth et al. 2004).

Parental monitoring and supervision are critical for drug abuse prevention. These skills can be enhanced with training on rule-setting; techniques for monitoring activities; praise for appropriate behavior; and moderate, consistent discipline that enforces defined family rules (Kosterman et al. 2001).

Drug education and information for parents or caregivers reinforces what children are learning about the harmful effects of drugs and opens opportunities for family discussions about the abuse of legal and illegal substances (Bauman et al. 2001).

Brief, family-focused interventions for the general population can positively change specific parenting behavior that can reduce later risks of drug abuse (Spoth et al. 2002b).

Principle 6 - Prevention programs can be designed to intervene as early as infancy to address risk factors for drug abuse, such as aggressive behavior, poor social skills, and academic difficulties (Webster-Stratton 1998; Olds et al. 1998; Webster-Stratton et al. 2001; Fisher et al. 2007).

Principle 7 - Prevention programs for elementary school children should target improving academic and social-emotional learning to address risk factors for drug abuse, such as early aggression, academic failure, and school dropout. Education should focus on the following skills (Conduct Problems Prevention Research Group 2002; Ialongo et al. 2001; Riggs et al. 2006; Kellam et al. 2008; Beets et al. 2009):

- self-control
- emotional awareness
- communication
- social problem-solving
- academic support, especially in reading

Principle 8 - Prevention programs for middle or junior high and high school students should increase academic and social competence with the following skills (Botvin et al. 1995; Scheier et al. 1999; Eisen et al. 2003; Ellickson et al. 2003; Haggerty et al. 2007):

- study habits and academic support
- communication
- peer relationships
- self-efficacy and assertiveness

- drug resistance skills
- reinforcement of anti-drug attitudes
- strengthening of personal commitments against drug abuse

Principle 9 - Prevention programs aimed at general populations at key transition points, such as the transition to middle school, can produce beneficial effects even among high-risk families and children. Such interventions do not single out risk populations and, therefore, reduce labeling and promote bonding to school and community (Botvin et al. 1995; Dishion et al. 2002; Institute of Medicine 2009).

Principle 10 - Community prevention programs that combine two or more effective programs, such as family-based and school-based programs, can be more effective than a single program alone (Battistich et al. 1997; Spoth et al. 2002c; Stormshak et al. 2005).

Principle 11 - Community prevention programs reaching populations in multiple settings—for example, schools, clubs, faith-based organizations, and the media—are most effective when they present consistent, community-wide messages in each setting (Chou et al. 1998; Hawkins et al. 2009).

Principle 12 - When communities adapt programs to match their needs, community norms, or differing cultural requirements, they should retain core elements of the original research-based intervention (Spoth et al. 2002b; Hawkins et al. 2009), which include:

- structure (how the program is organized and constructed)
- content (the information, skills, and strategies of the program)
- delivery (how the program is adapted, implemented, and evaluated)

Principle 13 - Prevention programs should be long-term with repeated interventions (i.e., booster programs) to reinforce the original prevention goals. Research shows that the benefits from middle school prevention programs diminish without follow-up programs in high school (Botvin et al. 1995; Scheier et al. 1999).

Principle 14 - Prevention programs should include teacher training on good classroom management practices, such as rewarding appropriate student behavior. Such techniques

help to foster students' positive behavior, achievement, academic motivation, and school bonding (Ialongo et al. 2001; Kellam et al. 2008).

Principle 15 - Prevention programs are most effective when they employ interactive techniques, such as peer discussion groups and parent role-playing, that allow for active involvement in learning about drug abuse and reinforcing skills (Botvin et al. 1995).

Principle 16 - Research-based prevention programs can be cost-effective. Similar to earlier research, recent research shows that for each dollar invested in prevention, a savings of up to $10 in treatment for alcohol or other substance abuse can be seen (Aos et al. 2001; Hawkins et al. 1999; Pentz 1998; Spoth et al. 2002a; Jones et al. 2008; Foster et al. 2007; Miller and Hendrie 2009).

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B. Substance Use and Military Life

General Risk of Substance Use Disorders

The stresses of deployments and the unique culture of the military offer both risks and protective factors related to substance use among active duty personnel.1 Deployment is associated with smoking initiation, unhealthy drinking, drug use and risky behaviors.1 Zero-tolerance policies, lack of confidentiality and mandatory random drug testing that might deter drug use can also add to stigma, and could discourage many who need treatment from seeking it. For example, half of military personnel have reported that they believe seeking help for mental health issues would negatively affect their military career.1 However, overall, illicit drug use among active duty personnel is relatively low2 and cigarette smoking and misuse of prescription drugs have decreased in recent years.2 In contrast, rates of binge drinking are high compared to the general population.2

Service members can face dishonorable discharge and even criminal prosecution for a positive drug test, which can discourage illicit drug use. Once active duty personnel leave the military some protective influences are gone, and substance use and other mental health issues become of greater concern.

More than one in ten veterans have been diagnosed with a substance use disorder, slightly higher than the general population.3 One study found that the overall prevalence of substance use disorders (SUDs) among male veterans was lower than rates among their civilian counterparts when all ages were examined together. However, when looking at the pattern for only male veterans aged 18–25 years, the rates were higher in veterans compared with civilians.3 The veteran population is also greatly impacted by several critical issues related to substance use, such as pain, suicide risk, trauma, and homelessness.

Illicit drugs

Among Active Duty Personnel:

Rates of illicit drug use among active duty service members have decreased in recent years and were at lower levels in the 2015 Health Related Behaviors Survey (HRBS) compared to the 2011 survey. The HRBS is the flagship survey for understanding the health, health-related behaviors and well-being of service members funded by the Department of Defense. It should be noted that the survey relies on self-reporting, and response rate is low, at 8.6%.2 However, it does provide a glimpse into substance use among active duty personnel.

The 2015 survey reported that illicit drug use in the past year was reported by less than 1 percent across all service branches and among both enlisted personnel and officers.2 By

comparison, a large government self-reported survey of civilians suggests about 1 in 5 young adults aged 18 to 25 (22.3%) were current users of illicit drugs in 2015.12

Veterans:
Reported rates of illicit drug use increase when active duty personnel leave military service. Marijuana accounts for the vast majority of illicit drug use among veterans with 3.5% reporting use, and 1.7% reporting use of illicit drugs other than marijuana in a 1-month period.3 From 2002 to 2009, cannabis use disorders increased more than 50% among veterans treated by in the Veterans Health Administration (VHA) system.3 Other illicit drugs are of concern for some veterans. One government report notes that more than ten percent of veteran admissions to substance use treatment centers were for heroin (10.7%), followed by cocaine at just over 6%.5

Opioid and other Prescription Drug Misuse
Active Duty:
Among active-duty service members in the 2015 HRBS, just over 4% reported misusing one or more prescription drug types in the past year.2

There has been much discussion about the amount of prescription pain medications prescribed to injured and sick military personnel, especially during the transition to medical discharge.1 Military physicians wrote nearly 3.8 million prescriptions for pain medication in 2009, more than quadruple the number of such prescriptions written in 2001.6 However, in the past few years, self-reported use of both prescription opioid pain relievers and use of sedatives has decreased among active duty personnel. From 2011 to 2015, the percentage of service members using pain relievers in the past month decreased by nearly half, likely reflecting prevention and appropriate prescribing initiatives set in motion by the Department of Defense.22 Nonetheless, these medications were misused and overused more often than other drugs. Prescription drug misuse was highest in the Army and lowest in the Coast Guard.2

Opioid use disorders among military personnel often begin with a opioid pain prescription following an injury during deployment. However, due to the addictive nature of opioids, particularly coupled with mental health struggles experienced by some military service men and women, regular use of opioids can lead to addiction.

Veterans:

Many veterans have unique issues related to pain management, with two-thirds reporting they experience pain.7 More than 9% reported that they experience severe pain, compared to only 6.4% of non-veterans7, putting them at higher risk for accidental opioid pain reliever overdoses. From 2001 to 2009, the percent of veterans in the VHA system receiving an opioid prescription increased from 17% to 24%.3 Similarly, the overall opioid overdose rates of veterans increased to 21% in 2016 from 14% in 2010.8 However, the overdose increases were mostly from heroin and synthetic opioids, and not from opioids taken for pain relief.8

Alcohol

Active Duty:

Alcohol use disorders are the most prevalent form of SUDs among military personnel.5 It is challenging to compare overall rates to the non military population because service personnel tend to be younger and have a higher percentage of males, putting them at greater risk in general. 2 However, increased combat exposure involving violence and trauma experienced by those who serve result in an increased risk of problematic drinking. The 2015 HRBS report concluded that across all services, 5.4 percent of military personnel were heavy drinkers compared to 6.7 percent in the general adult population reported in 2014. However, binge drinking was reported as higher among active duty personnel (30% vs. 24.7%), although lower than the 33% reported in 2011. 2 One in three of service members were binge drinkers, comparable to a 2014 estimate of one in four in the general population.2 More than one in three service personnel met criteria for hazardous drinking or possible alcohol use disorder,2 with rates higher among men than women.

Veterans:

A 2017 study examining National Survey on Drug Use and Health data found that, compared to their non-veteran counterparts, veterans were more likely to use alcohol (56.6% vs 50.8% in a 1-month period), and to report heavy use of alcohol (7.5% vs 6.5% in a 1-month period).3 Sixty-five percent of veterans who enter a treatment program report alcohol as the substance they most frequently misuse, which is almost double that of the general population.5

Smoking

Active Duty:

Deployment and combat exposure puts service personnel at risk for smoking initiation, but rates have decreased in recent years.1 The 2015 HRBS report showed that close to 14% of service members were current cigarette smokers and more than 7% smoke daily.2 This roughly compares to a rate of 15% of current smokers in the general U.S. adult population in 2015, with 11% smoking daily.4 The 2015 rates in the military represent a decrease from 24%

in 2011 (with 13% reported as daily smokers.)2 The 2015 report also showed that nearly 9% of military service personnel were current cigar smokers and nearly 13% used smokeless tobacco.2 Close to 40% of those who smoke started after enlisting, underscoring the need for prevention strategies for new active duty personnel.9 The Department of Defense offers smoking cessation programs, and in 2016 prohibited tobacco use on its medical facilities, with a goal to achieve tobacco-free installations by 2020.9

Veterans:
Data suggests that veterans are more likely to use tobacco products than their non-veteran counterparts in nearly all age groups,9 with close to 30% reporting use.9 The high prevalence of tobacco use among people with military experience has had a significant financial impact on the VHA, costing an estimated $2.7 billion (7.6% of its expenditures) on smoking-related ambulatory care, prescription drugs, hospitalization, and home health care.9

In addition, a higher proportion of veterans with coronary heart disease are smokers compared to civilians with similar diagnoses.10 For those without heart disease, veterans are more likely to be former smokers than all civilians.10 In recent years, the VHA has made efforts to increase access to tobacco cessation treatment options,9 yielding some results.

Vaping and E-Cigarettes:
The 2015 HRBS report asked about e-cigarettes; however, the information is now several years old, with a new report in development. Even in 2015, 12.4 percent of service members reported they had vaped within the last month, with 11.1 percent saying they were daily e-cigarette users2, roughly compared to 3.7% reporting regular use in the general population in 2014.26

In 2017, the U.S. Navy issued a report that there had been more than 15 mishaps with vaping devices causing personal injuries or fire damage, about half happening on board Navy vessels or aircraft. As a result, e-cigarettes were banned throughout the fleet.27
With the growing number of serious lung illnesses and deaths related to vaping reported in 2019, service members and their families were officially alerted about the dangers, and encouraged not to use e-cigarette products.28 Subsequently, in October 2019 the Army, Air Force and Navy banned sales of vaping devices from retail exchanges on bases.29

Substance Use, Mental Health and Military/Veteran Life
All veterans experience a period of readjustment as they leave the military and reintegrate into life with family, friends, and their community, leaving them with unique mental health

challenges.11 A number of environmental stressors specific to military personnel have been linked to increased risk of SUDs among military personnel and veterans, including deployment, combat exposure, and post-deployment civilian/reintegration challenges.3 Among veterans presenting for first-time care within the VHA system, close to 11% meet criteria for an SUD diagnosis.3 Veterans with SUDS commonly meet the criterial for co-occurring mental health disorders such as PTSD, depression and anxiety.3

Those who have experienced trauma or were hospitalized or injured during combat are at risk for increased drinking or drug use. Veterans with SUDs are 3-4 times more likely to receive a PTSD or depression diagnosis.3

It is estimated that between 37 and 50 percent of Afghanistan and Iraq War veterans have been diagnosed with a mental disorder.11 These conditions are strongly associated with substance use disorders (SUDs), as are other problems experienced by returning military personnel, including reintegration stresses, sleep disturbances, traumatic brain injury (TBI), and violence in relationships. Onset of SUDs can also emerge secondary to other mental health problems associated with these stressors, such as post-traumatic stress disorder (PTSD) and depression.3

SUDs, PTSD and Depression

Among recent Afghanistan and Iraq veterans, 63% diagnosed with SUDs also met criteria for post-traumatic stress disorder (PTSD).3 Veterans dually diagnosed with PTSD and SUDs are more likely to have additional co-occurring psychiatric and medical conditions, such as seizures, liver disease, HIV, schizophrenia, anxiety disorders, and bipolar disorder.3

Counseling

Research suggests that relatively few service members receive counseling related to SUDs, however there are few studies on SUD services received in the military.1 Behavioral interventions for the management of SUDs typically involve short-term, cognitive-behavioral therapy interventions. These interventions focus on the identification and modification of maladaptive thoughts and behaviors associated with increased craving, use, or relapse to substances. With some drugs–opioids, alcohol, and tobacco—behavioral counseling is an effective companion to approved medication therapy. With other drugs, such as cocaine and marijuana, there are no approved medicines for treatment, making behavioral counseling the focus of treatment. The military offers free counseling services for alcohol and substance use disorders, including smoking cessation support. There are also several services and

interventions available to help reduce SUDs among veterans, including both behavioral and pharmacological treatments.

Suicide

Suicide deaths among active duty military and veterans exceed the rate for the general population. In 2014, veterans comprised more than 20 percent of national suicides, with an average of 20 veterans dying by suicide every day.14 In 2016, the suicide rate was 1.5 times greater for veterans than for non-veteran adults, after adjusting for age and gender.13

Substance use often precedes suicidal behavior in the military. About 30% of Army suicides and over 45% of suicide attempts since 2003 involved alcohol or drug use.3 In addition, an estimated 20% of high-risk behavior deaths were attributed to alcohol or drug overdose.3 Researchers have looked at the possible link between suicide, pain and prescription pain medications. In a 2017 VA study of nearly 124,000 veterans, those receiving the highest doses of opioid pain relievers were more than twice as likely to die by suicide, compared with those receiving the lowest doses.15 But most of those suicides are with firearms, not opioids, and it is unclear if there's a direct causal link between the pain medications and suicide risk or if the high doses may be a marker for other factors that drive suicide—including unresolved severe chronic pain.15

Homelessness

U.S. military veterans are estimated to be a large portion (around 11 percent) of homeless adults.17 According to a 2014 study, around 70 percent of homeless veterans also have a substance use disorder.16

In 2011, about one fifth of veterans in substance use treatment were homeless.16 These homeless veterans experience unique challenges and barriers to substance use disorder treatment. Targeting homeless veterans in need of treatment so that they can receive support through outreach services, case management, and housing assistance can improve their chances of entering substance use treatment and experiencing positive outcomes.16

Addressing the Problem

A 2012 Institute of Medicine (IOM) report identified a number of barriers to substance use disorder care among active duty military personnel and veterans, including limited access to treatment, gaps in insurance coverage, stigma, fear of negative consequences, and lack of confidential services. The report offered remedies, including increasing the use of evidence-based prevention and treatment interventions and expanding access to care. The report also recommended broadening insurance coverage to include effective outpatient treatments

and better equipping health care providers to recognize and screen for substance use problems so they can refer patients to appropriate, evidence-based treatment when needed. The IOM report also notes that addressing substance use in the military will require increasing confidentiality and shifting a cultural climate in which drug problems can be stigmatized and evoke fear in people suffering from them.6

In 2013, the VHA began the Opioid Safety Initiative, a multifaceted for chronic pain,18 and has increased its resources for consumers, including 21 intervention that has been associated witha16% reduction in opioid prescribing in the first two years.[22]The VHA also recently revised its clinical practice guidelines for prescribing opioids for chronic pain,[18]and has increased its resources for consumers, including a consumer fact sheet on safe and responsible use of opioids for chronic pain.[21]
In 2016, the military's Tricare health system for active duty personnel announced it was expanding its treatment services to include intensive outpatient programs.[20]Its health system web site now offers an alcohol and drug use assessment tool at
https://www.health.mil/Military-Health-Topics/Conditions-and-Treatments/Substance-Abuse.

The Veterans Administration has also developed the National Strategy for Preventing Veteran Suicide, which provides a framework for identifying priorities, organizing efforts, and contributing to a national focus on veteran suicide prevention.[13]From 2015-2016, the number of suicides per year among veterans decreased.[13]

Treatment

Treatment for various substance use and mental disorders are available through military health systems and have been shown to be effective. Treatments include behavioral interventions and medicines when available. All treatment should be individualized, including approved medication options approved for patients with alcohol, nicotine and opioid use disorders.

There are three FDA-approved medicines to treat opioid addiction, offering options to meet individual needs. Buprenorphine and methadone are medicines that bind to the same receptors in the brain as opioids, called opioid agonists or partial agonists. Naltrexoneis another medication that treats opioid addiction, but it is called an antagonist, preventing opioids from having an effect on the brain. Additionally, the Food and Drug Administration recently approved a medicine called lofexidine to help make withdrawal

symptoms easier for people who are trying to stop using opioids, which should be followed with engagement in treatment.

While many treatment centers do not offer these medications, the National Academy of Sciences recently issued a scientific report stating that medications for opioid use disorder are effective, save lives and have better long-term outcomes than treatment that does not include medications.[23] A combination of medication with behavioral therapy can reinforce treatment goals, rebuild relationships with friends and family, and build healthy life skills.

The Veterans Health Administration acknowledges that treatment with medications for opioid use disorder, including opioid agonists (methadone or buprenorphine), is the first-line treatment for opioid use disorder and recommends it for all opioid-dependent patients. Notably, a 2015 revision of treatment guidelines for the U.S. Department of Veteran Affairs and U.S. Department of Defense shifted toward allowing these medications as a treatment option for active duty military members.[18] However, despite evidence of effectiveness, these medications are prescribed to fewer than 35% of Veterans Health Administration patients diagnosed with opioid use disorder.[19] Barriers to opioid agonist medication among VHA providers include lack of perceived patient interest, stigma toward the patient population, and lack of education about opioid agonist treatment.

Families with loved ones with opioid use disorders should investigate having the medicine naloxoneon hand to reverse an opioid overdose. An easy-to-use nasal spray is available at many pharmacies without personal prescriptions.

Current Research

NIDA and other government agencies continue to research strategies for managing substance use disorders and related mental health issues in people with military experience. The research questions can be complex and vary with different population subtypes, and can reveal the need for additional research directions. For example, a 2019 study looked at the effectiveness of integrating treatment for both SUDs and PTSD, concluding that veterans with PTSD and co-occurring polysubstance use issues (as compared to a single substance use issue) may experience greater improvement in substance use but less improvement in PTSD symptoms.24 Another 2019 study identified chronic pain as a common condition among polysubstance users and showed the importance of incorporating interdisciplinary pain management approaches during treatment to reduce reliance on long-term opioid therapy and improve rehabilitation.25 NIDA will continue to focus on developing evidence-based strategies to help this population return to productive military and civilian lives.

Resources for Military Members, Veterans, and their families

• Veterans Crisis Line/Suicide Hotline: 1-800-(273)-8255 or send a text message to 838255

• Resources for homeless in your community: https://www.samhsa.gov/homelessness-programs-resources/hpr-resources

• Where to find opioid overdose reversal medication, naloxone: http://www.getnaloxonenow.org/

• U.S Department of Veterans Affairs: https://www.va.gov/

• FREE VA online resource for military members concerned about their drinking: https://www.ptsd.va.gov/apps/change/

• Alcohol Treatment Navigator (NIAAA) https://alcoholtreatment.niaaa.nih.gov/

• Opioid Safety Initiative Toolkit (for consumers and clinicians) https://www.va.gov/PAINMANAGEMENT/Opioid_Safety_Initiative_OSI.asp

• For military family support: https://www.med.navy.mil/sites/nmcphc/Documents/health-promotion-wellness/psychological-emotional-wellbeing/DSPOFamilyGuide.pdf

• VA/DoD Clinical Practice Guidelines for the Management of Substance Use Disorders https://www.healthquality.va.gov/guidelines/Pain/cot/

• SAMHSA-HRSA Veterans Resource Guide: https://www.integration.samhsa.gov/clinical-practice/Veterans_Resource_Guide_FINAL.pdf

• Substance Use Treatment for Veterans: https://www.va.gov/health-care/health-needs-conditions/substance-use-problems/

• Current Research and Resources from NIDA: https://www.drugabuse.gov/related-topics/military

• Military One Source: https://www.militaryonesource.mil/health-wellness

• Becoming a Smoke Free Veteran: https://veterans.smokefree.gov/

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.

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C. Treatment Approaches for Drug Addiction

What is drug addiction?

Drug addiction is a chronic disease characterized by compulsive, or uncontrollable, drug seeking and use despite harmful consequences and changes in the brain, which can be long lasting. These changes in the brain can lead to the harmful behaviors seen in people who use drugs. Drug addiction is also a relapsing disease. Relapse is the return to drug use after an attempt to stop.

The path to drug addiction begins with the voluntary act of taking drugs. But over time, a person's ability to choose not to do so becomes compromised. Seeking and taking the drug becomes compulsive. This is mostly due to the effects of long-term drug exposure on brain function. Addiction affects parts of the brain involved in reward and motivation, learning and memory, and control over behavior.

Addiction is a disease that affects both the brain and behavior.

Can drug addiction be treated?

Yes, but it's not simple. Because addiction is a chronic disease, people can't simply stop using drugs for a few days and be cured. Most patients need long-term or repeated care to stop using completely and recover their lives.

Addiction treatment must help the person do the following:

- stop using drugs
- stay drug-free
- be productive in the family, at work, and in society

Principles of Effective Treatment

Based on scientific research since the mid-1970s, the following key principles should form the basis of any effective treatment program:

- Addiction is a complex but treatable disease that affects brain function and behavior.
- No single treatment is right for everyone.
- People need to have quick access to treatment.
- Effective treatment addresses all of the patient's needs, not just his or her drug use.
- Staying in treatment long enough is critical.
- Counseling and other behavioral therapies are the most commonly used forms of treatment.
- Medications are often an important part of treatment, especially when combined with behavioral therapies.

- Treatment plans must be reviewed often and modified to fit the patient's changing needs.
- Treatment should address other possible mental disorders.
- Medically assisted detoxification is only the first stage of treatment.
- Treatment doesn't need to be voluntary to be effective.
- Drug use during treatment must be monitored continuously.
- Treatment programs should test patients for HIV/AIDS, hepatitis B and C, tuberculosis, and other infectious diseases as well as teach them about steps they can take to reduce their risk of these illnesses.

What are treatments for drug addiction?

There are many options that have been successful in treating drug addiction, including:

- behavioral counseling
- medication
- medical devices and applications used to treat withdrawal symptoms or deliver skills training
- evaluation and treatment for co-occurring mental health issues such as depression and anxiety
- long-term follow-up to prevent relapse

A range of care with a tailored treatment program and follow-up options can be crucial to success. Treatment should include both medical and mental health services as needed.

Follow-up care may include community- or family-based recovery support systems.

How are medications used in drug addiction treatment?

Medications can be used to manage withdrawal symptoms, prevent relapse, and treat co-occurring conditions.

Withdrawal. Medications help suppress withdrawal symptoms during detoxification. Detoxification is not in itself "treatment," but only the first step in the process. Patients who do not receive any further treatment after detoxification usually resume their drug use. One study of treatment facilities found that medications were used in almost 80 percent of detoxifications (SAMHSA, 2014). Devices are also being used to reduce withdrawal symptoms. In November 2017, the Food and Drug Administration (FDA) granted a new indication to an electronic stimulation device, NSS-2 Bridge, for use in helping reduce opioid

withdrawal symptoms. This device is placed behind the ear and sends electrical pulses to stimulate certain brain nerves.

Relapse prevention. Patients can use medications to help re-establish normal brain function and decrease cravings. Medications are available for treatment of opioid (heroin, prescription pain relievers), tobacco (nicotine), and alcohol addiction. Scientists are developing other medications to treat stimulant (cocaine, methamphetamine) and cannabis (marijuana) addiction. People who use more than one drug, which is very common, need treatment for all of the substances they use.

- ***Opioids:*** Methadone (Dolophine®, Methadose®), buprenorphine (Suboxone®, Subutex®, Probuphine® , Sublocade™), and naltrexone (Vivitrol®) are used to treat opioid addiction. Acting on the same targets in the brain as heroin and morphine, methadone and buprenorphine suppress withdrawal symptoms and relieve cravings. Naltrexone blocks the effects of opioids at their receptor sites in the brain and should be used only in patients who have already been detoxified. All medications help patients reduce drug seeking and related criminal behavior and help them become more open to behavioral treatments. A NIDA study found that once treatment is initiated, both a buprenorphine/naloxone combination and an extended release naltrexone formulation are similarly effective in treating opioid addiction. Because full detoxification is necessary for treatment with naloxone, initiating treatment among active users was difficult, but once detoxification was complete, both medications had similar effectiveness.

- ***Tobacco:*** Nicotine replacement therapies have several forms, including the patch, spray, gum, and lozenges. These products are available over the counter. The U.S. Food and Drug Administration (FDA) has approved two prescription medications for nicotine addiction: bupropion (Zyban®) and varenicline (Chantix®). They work differently in the brain, but both help prevent relapse in people trying to quit. The medications are more effective when combined with behavioral treatments, such as group and individual therapy as well as telephone quit lines.

- ***Alcohol:*** Three medications have been FDA-approved for treating alcohol addiction and a fourth, topiramate, has shown promise in clinical trials (large- scale studies with people). The three approved medications are as follows:

- **Naltrexone** blocks opioid receptors that are involved in the rewarding effects of drinking and in the craving for alcohol. It reduces relapse to heavy drinking and is highly effective in some patients. Genetic differences may affect how well the drug works in certain patients.
- **Acamprosate (Campral®)** may reduce symptoms of long-lasting withdrawal, such as insomnia, anxiety, restlessness, and dysphoria (generally feeling unwell or unhappy). It may be more effective in patients with severe addiction.
- **Disulfiram (Antabuse®)** interferes with the breakdown of alcohol. Acetaldehyde builds up in the body, leading to unpleasant reactions that include flushing (warmth and redness in the face), nausea, and irregular heartbeat if the patient drinks alcohol. Compliance (taking the drug as prescribed) can be a problem, but it may help patients who are highly motivated to quit drinking.

- ***Co-occuring conditions:*** Other medications are available to treat possible mental health conditions, such as depression or anxiety, that may be contributing to the person's addiction.

How are behavioral therapies used to treat drug addiction?

Behavioral therapies help patients:

- modify their attitudes and behaviors related to drug use
- increase healthy life skills
- persist with other forms of treatment, such as medication

Patients can receive treatment in many different settings with various approaches.

Outpatient behavioral treatment includes a wide variety of programs for patients who visit a behavioral health counselor on a regular schedule. Most of the programs involve individual or group drug counseling, or both. These programs typically offer forms of behavioral therapy such as:

- ***cognitive-behavioral therapy,*** which helps patients recognize, avoid, and cope with the situations in which they are most likely to use drugs
- ***multidimensional family therapy***—developed for adolescents with drug abuse problems as well as their families—which addresses a range of influences on their drug abuse patterns and is designed to improve overall family functioning

- ***motivational interviewing,*** which makes the most of people's readiness to change their behavior and enter treatment
- ***motivational incentives*** (contingency management), which uses positive reinforcement to encourage abstinence from drugs

Treatment is sometimes intensive at first, where patients attend multiple outpatient sessions each week. After completing intensive treatment, patients transition to regular outpatient treatment, which meets less often and for fewer hours per week to help sustain their recovery. In September 2017, the FDA permitted marketing of the first mobile application, reSET®, to help treat substance use disorders. This application is intended to be used with outpatient treatment to treat alcohol, cocaine, marijuana, and stimulant substance use disorders. In December 2018, the FDA cleared a mobile medical application, reSET®, to help treat opioid use disorders. This application is a prescription cognitive behavioral therapy and should be used in conjunction with treatment that includes buprenorphine and contingency management. Read more about reSET® in this FDA News Release.

Inpatient or residential treatment can also be very effective, especially for those with more severe problems (including co-occurring disorders). Licensed residential treatment facilities offer 24-hour structured and intensive care, including safe housing and medical attention. Residential treatment facilities may use a variety of therapeutic approaches, and they are generally aimed at helping the patient live a drug-free, crime-free lifestyle after treatment. Examples of residential treatment settings include:

- ***Therapeutic communities***, which are highly structured programs in which patients remain at a residence, typically for 6 to 12 months. The entire community, including treatment staff and those in recovery, act as key agents of change, influencing the patient's attitudes, understanding, and behaviors associated with drug use. Read more about therapeutic communities in the *Therapeutic Communities Research Report* at https://www.drugabuse.gov/publications/ research-reports/therapeutic-communities.
- ***Shorter-term residential treatment***, which typically focuses on detoxification as well as providing initial intensive counseling and preparation for treatment in a community-based setting.
- ***Recovery housing,*** which provides supervised, short-term housing for patients, often following other types of inpatient or residential treatment. Recovery housing can help people make the transition to an independent life—for example, helping them learn how to manage finances or seek employment, as well as connecting them to support services in the community.

Is treatment different for criminal justice populations?

Scientific research since the mid-1970s shows that drug abuse treatment can help many drug-using offenders change their attitudes, beliefs, and behaviors towards drug abuse; avoid relapse; and successfully remove themselves from a life of substance abuse and crime. Many of the principles of treating drug addiction are similar for people within the criminal justice system as for those in the general population. However, many offenders don't have access to the types of services they need. Treatment that is of poor quality or is not well suited to the needs of offenders may not be effective at reducing drug use and criminal behavior.

In addition to the general principles of treatment, some considerations specific to offenders include the following:

- Treatment should include development of specific cognitive skills to help the offender adjust attitudes and beliefs that lead to drug abuse and crime, such as feeling entitled to have things one's own way or not understanding the consequences of one's behavior. This includes skills related to thinking, understanding, learning, and remembering.
- Treatment planning should include tailored services within the correctional facility as well as transition to community-based treatment after release.
- Ongoing coordination between treatment providers and courts or parole and probation officers is important in addressing the complex needs of offenders re-entering society.

Challenges of Re-entry

Drug abuse changes the function of the brain, and many things can "trigger" drug cravings within the brain. It's critical for those in treatment, especially those treated at an inpatient facility or prison, to learn how to recognize, avoid, and cope with triggers they are likely to be exposed to after treatment.

How many people get treatment for drug addiction?

According to SAMHSA's National Survey on Drug Use and Health, 22.5 million people (8.5 percent of the U.S. population) aged 12 or older needed treatment for an illicit* drug or alcohol use problem in 2014. Only 4.2 million (18.5 percent of those who needed treatment) received any substance use treatment in the same year. Of these, about 2.6 million people received treatment at specialty treatment programs (CBHSQ, 2015).

*The term "illicit" refers to the use of illegal drugs, including marijuana according to federal law, and misuse of prescription medications.

Points to Remember

- Drug addiction can be treated, but it's not simple. Addiction treatment must help the person do the following:
  - stop using drugs
  - stay drug-free
  - be productive in the family, at work, and in society

- Successful treatment has several steps:
  - detoxification
  - behavioral counseling
  - medication (for opioid, tobacco, or alcohol addiction)
  - evaluation and treatment for co-occurring mental health issues such as depression and anxiety
  - long-term follow-up to prevent relapse

- Medications and devices can be used to manage withdrawal symptoms, prevent relapse, and treat co-occurring conditions.
- Behavioral therapies help patients:
  - modify their attitudes and behaviors related to drug use
  - increase healthy life skills
  - persist with other forms of treatment, such as medication
- People within the criminal justice system may need additional treatment services to treat drug use disorders effectively. However, many offenders don't have access to the types of services they need.

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.
Updated January 2019

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Chapter 5 - Medications for Opioid Use Disorder

[Chapter 5 is taken from TIP 63, Substance Abuse and Mental Health Services Administration (SAMHSA), Department of Health & Human Services, www.samhsa.gov]

A. Introduction to Medications for Opioid Use Disorder Treatment

The goal of treatment for opioid addiction or opioid use disorder (OUD) is remission of the disorder leading to lasting recovery. Recovery is a process of change through which individuals improve their health and wellness, live self-directed lives, and strive to reach their full potential.[64] This Treatment Improvement Protocol (TIP) reviews the use of the three Food and Drug Administration (FDA)-approved medications used to treat OUD—methadone, naltrexone, and buprenorphine—and the other strategies and services needed to support recovery for people with OUD.

Introduction

Our nation faces a crisis of overdose deaths from opioids, including heroin, illicit fentanyl, and prescription opioids. These deaths represent a mere fraction of the total number of Americans harmed by opioid misuse and addiction. Many Americans now suffer daily from a chronic medical illness called "opioid addiction" or OUD. Healthcare professionals, treatment providers, and policymakers have a responsibility to expand access to evidence-based, effective care for people with OUD.

An expert panel developed the TIP's content based on a review of the literature and on their extensive experience in the field of addiction treatment. Other professionals also generously contributed their time and commitment to this project.

Overall Key Messages

Addiction is a chronic, treatable illness.

Opioid addiction, which generally corresponds with moderate to severe forms of OUD, often requires continuing care for effective treatment rather than an episodic, acute-care treatment approach.

[64] Substance Abuse and Mental Health Services Administration. (2017). Recovery and recovery support [Webpage]. Retrieved November 17, 2017, from www.samhsa.gov/recovery

General principles of good care for chronic diseases can guide OUD treatment. Approaching OUD as a chronic illness can help providers deliver care that helps patients stabilize, achieve remission of symptoms, and establish and maintain recovery.

Patient-centered care empowers patients with information that helps them make better treatment decisions with the healthcare professionals involved in their care. Patients should receive information from their healthcare team that will help them understand OUD and the options for treating it, including treatment with FDA-approved medication.

Patients with OUD should have access to mental health services as needed, medical care, and addiction counseling, as well as recovery support services, to supplement treatment with medication.

The words you use to describe OUD and an individual with OUD are powerful. The TIP defines, uses, and encourages providers to adopt terminology that will not reinforce prejudice, negative attitudes, or discrimination.

There is no "one size fts all" approach to OUD treatment. Many people with OUD benefit from treatment with medication for varying lengths of time, including lifelong treatment. Ongoing outpatient medication treatment for OUD is linked to better retention and outcomes than treatment without medication. Even so, some people stop using opioids on their own; others recover through support groups or specialty treatment with or without medication.

The science demonstrating the effectiveness of medication for OUD is strong. For example, methadone, extended-release injectable naltrex-one (XR-NTX), and buprenorphine were each found to be more effective in reducing illicit opioid use than no medication in randomized clinical trials, which are the gold standard for demonstrating efficacy in clinical

medicine.[65] [66] [67] [68] [69] Methadone and buprenorphine treatment have also been associated with reduced risk of overdose death.[70] [71] [72] [73] [74]

This doesn't mean that remission and recovery occur only through medication. Some people achieve remission without OUD medication, just as some people can manage type 2 diabetes with exercise and diet alone. But just as it is inadvisable to deny people with diabetes the medication they need to help manage their illness, it is also not sound medical practice to deny people with OUD access to FDA-approved medications for their illness.

Medication for OUD should be successfully integrated with outpatient and residential treatment. Some patients may benefit from different levels of care at different points in their lives, such as outpatient counseling, intensive outpatient treatment, inpatient treatment, or long-term therapeutic communities. Patients treated in these settings should have access to OUD medications.

Patients treated with medications for OUD can benefit from individualized psychosocial supports. These can be offered by patients' healthcare providers in the form of medication management and supportive counseling and/or by other providers offering adjunctive addiction counseling, recovery coaching, mental health services, and other services that may be needed by particular patients.

Expanding access to OUD medications is an important public health strategy.[75] The gap between the number of people needing opioid addiction treatment and the capacity to treat them with OUD medication is substantial. In 2012, the gap was estimated at nearly 1 million

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[65] Johnson, R. E., Chutuape, M. A., Strain, E. C., Walsh, S. L., Stitzer, M. L., & Bigelow, G. E. (2000). A comparison of levomethadyl acetate, buprenorphine, and methadone for opioid dependence. *New England Journal of Medicine, 343*(18), 1290–1297.

[66] Krupitsky, E., Nunes, E. V., Ling, W., Illeperuma, A., Gastfriend, D. R., & Silverman, B. L. (2011, April 30). Injectable extended-release naltrexone for opioid dependence: A double-blind, placebo-controlled, multicentre randomised trial. *Lancet, 377*(9776), 1506–1513.

[67] Lee, J. D., Friedmann, P. D., Kinlock, T. W., Nunes, E. V., Boney, T. Y., Hoskinson, R. A., Jr., … O'Brien, C. P. (2016). Extended-release naltrexone to prevent opioid relapse in criminal justice offenders. *New England Journal of Medicine, 374*(13), 1232–1242.

[68] Mattick, R. P., Breen, C., Kimber, J., & Davoli, M. (2009). Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. *Cochrane Database of Systematic Reviews, 2009*(3), 1–19.

[69] Mattick, R. P., Breen, C., Kimber, J., & Davoli, M. (2014). Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *Cochrane Database of Systematic Reviews, 2014*(2), 1–84.

[70] Auriacombe, M., Fatséas, M., Dubernet, J., Daulouède, J. P., & Tignol, J. (2004). French feld experience with buprenorphine. *American Journal on Addictions, 13*(Suppl. 1), S17–S28.

[71] Degenhardt, L., Randall, D., Hall, W., Law, M., Butler, T., & Burns, L. (2009). Mortality among clients of a state-wide opioid pharmacotherapy program over 20 years: Risk factors and lives saved. *Drug and Alcohol Dependence, 105*(1–2), 9–15.

[72] Gibson, A., Degenhardt, L., Mattick, R. P., Ali, R., White, J., & O'Brien, S. (2008). Exposure to opioid maintenance treatment reduces long-term mortality. *Addiction, 103*(3), 462–468.

[73] Schwartz, R. P., Gryczynski, J., O'Grady, K. E., Sharfstein, J. M., Warren, G., Olsen, Y., … Jaffe, J. H. (2013). Opioid agonist treatments and heroin overdose deaths in Baltimore, Maryland, 1995–2009. *American Journal of Public Health, 103*(5), 917–922.

[74] World Health Organization. (2009). *Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence.* Geneva, Switzerland: WHO Press.

[75] Department of Health and Human Services, Offce of the Surgeon General. (2016). *Facing addiction in America: The Surgeon General's report on alcohol, drugs, and health.* Washington, DC: Department of Health and Human Services.

people, with about 80 percent of opioid treatment programs (OTPs) nationally operating at 80 percent capacity or greater.[76]

Improving access to treatment with OUD medications is crucial to closing the wide gap between treatment need and treatment availability, given the strong evidence of effectiveness for such treatments.[77]

Data indicate that medications for OUD are cost effective and cost beneficial.[78] [79]

B. Key Terms

Addiction: As defined by the American Society of Addiction Medicine, "a primary, chronic disease of brain reward, motivation, memory, and related circuitry."[80] It is 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.** The *Diagnostic and Statistical Manual of Mental Disorders,* Fifth Edition[4] (DSM-5), does not use the term for diagnostic purposes, but it commonly describes the more severe forms of OUD.

Medically supervised withdrawal (formerly called detoxification): Using an opioid agonist (or an alpha-2 adrenergic agonist if an opioid agonist is not available) in tapering doses or other medications to help a patient discontinue illicit or prescription opioids.

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. Mu-opioid receptor full agonists (e.g., methadone) bind to the mu-opioid receptor and produce actions similar to those produced by the endogenous opioid beta-endorphin. Increasing the dose increases the effect. Mu-opioid receptor partial agonists (e.g., buprenorphine) bind to the mu-opioid receptor. Unlike with full agonists, increasing their

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[76] Jones, C. M., Campopiano, M., Baldwin, G., & McCance-Katz, E. (2015). National and state treatment need and capacity for opioid agonist medication-assisted treatment. *American Journal of Public Health, 105*(8), e55–e63.

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dose may not produce additional effects once they have reached their maximal effect. At low doses, partial agonists may produce effects similar to those of full agonists.

Opioid receptor antagonist: A substance that has affinity for opioid receptors in the CNS without producing the physiological effects of opioid agonists. Mu-opioid receptor antagonists (e.g., naltrexone) can block the effects of exogenously administered opioids.

Opioids: All natural, synthetic, and semisynthetic substances that have effects similar to morphine. They can be used as medications having such effects (e.g., methadone, buprenorphine, oxycodone).

Opioid treatment program (OTP): An accredited treatment program with SAMHSA certification and Drug Enforcement Administration registration to administer and dispense opioid agonist medications that are approved by FDA to treat opioid addiction. Currently, these include methadone and buprenorphine products. Other pharmacotherapies, such as naltrexone, may be provided but are not subject to these regulations. OTPs must provide adequate medical, counseling, vocational, educational, and other assessment and treatment services either onsite or by referral to an outside agency or practitioner through a formal agreement.

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. Tolerance and withdrawal do not count toward the diagnosis in people experiencing these symptoms when using opioids under appropriate medical supervision. OUD covers a range of severity and replaces what DSM-IV termed "opioid abuse" and "opioid dependence." An OUD diagnosis is applicable to a person who uses opioids and experiences at least 2 of the 11 symptoms in a 12-month period. (See Exhibit 2.13 in Part 2 for full DSM-5 diagnostic criteria for OUD.)

Recovery: A process of change through which individuals improve their health and wellness, live self-directed lives, and strive to reach their full potential. Even individuals with severe and chronic SUDs can, with help, overcome their SUDs and regain health and social function. Although abstinence from all substance misuse is a cardinal feature of a recovery lifestyle, it is not the only healthy, prosocial feature. Patients taking FDA-approved medication to treat OUD can be considered in recovery.

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. The TIP uses relapse to describe relapse prevention, a common treatment modality.

Remission: A medical term meaning a disappearance of signs and symptoms of the disease.[7] 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).[8] Remission is an essential element of **recovery.**

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.**

As is true for patients undergoing treatment for any chronic medical condition, patients with OUD should have access to medical, mental health, addiction counseling, and recovery support services that they may need to supplement treatment with medication. Medical care should include preventive services and disease management. Patients with OUD who have mental disorders should have access to mental health services.

Treatment and support services should reflect each patient's individual needs and preferences. Some patients, particularly those with co-occurring disorders, may require these treatments and services to achieve sustained remission and recovery.

The words you use to describe both OUD and an individual with OUD are powerful and can reinforce prejudice, negative attitudes, and discrimination. Negative attitudes held by the public and healthcare professionals can deter people from seeking treatment, make patients leave treatment prematurely, and contribute to worse treatment outcomes. The TIP expert panel recommends that providers always use medical terms when discussing SUDs (e.g., positive or negative urine sample, not dirty or clean sample) and use person-first language (e.g., a person with an SUD, not a user, alcoholic, or addict).

C. Overview of Medications for OUD

There is no "one size fits all" approach to OUD treatment. Many people with OUD benefit from treatment with medication for varying lengths of time, including lifelong treatment. Ongoing outpatient medication treatment for OUD is linked to better retention and outcomes than treatment without medication. Even so, some people stop using opioids on their own; others recover through support groups or specialty outpatient or residential treatment with or without medication. Still, FDA-approved medication should be considered and offered to patients with OUD as part of their treatment.

Benefits

The three FDA-approved medications used to treat OUD improve patients' health and wellness by:

- Reducing or eliminating withdrawal symptoms: methadone, buprenorphine.

- Blunting or blocking the effects of illicit opioids: methadone, naltrexone, buprenorphine.
- Reducing or eliminating cravings to use opioids: methadone, naltrexone, buprenorphine.

See Exhibit 1.2 for further comparison between these medications.

Effectiveness

The science demonstrating the effectiveness of medication for OUD is strong. For example, methadone, extended-release injectable naltrex-one (XR-NTX), and buprenorphine were each found to be more effective in reducing illicit opioid use than no medication in randomized clinical trials,[81] [82] [83] [84]which are the gold standard for demonstrating efficacy in clinical medicine. Methadone and buprenorphine treatment have also been associated with reduced risk of overdose death.[85] [86] [87] [88] [89]

Exhibit 1.2 Comparison of Medications for OUD

PRESCRIBING CONSIDERATIONS	METHADONE	NALTREXONE	BUPRENORPHINE
Mechanism of Action at mu-Opioid Receptor	Agonist	Antagonist	Partial agonist
Phase of Treatment	Medically supervised withdrawal, maintenance	Prevention of relapse to opioid dependence, following medically	Medically supervised withdrawal, maintenance

[81] Krupitsky, E., Nunes, E. V., Ling, W., Illeperuma, A., Gastfriend, D. R., & Silverman, B. L. (2011, April 30). Injectable extended-release naltrexone for opioid dependence: A double-blind, placebo-controlled, multicentre randomised trial. *Lancet, 377*(9776), 1506–1513.

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[83] Mattick, R. P., Breen, C., Kimber, J., & Davoli, M. (2009). Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. *Cochrane Database of Systematic Reviews, 2009*(3), 1–19.

[84] Mattick, R. P., Breen, C., Kimber, J., & Davoli, M. (2014). Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *Cochrane Database of Systematic Reviews, 2014*(2), 1–84.

[85] Auriacombe, M., Fatséas, M., Dubernet, J., Daulouède, J. P., & Tignol, J. (2004). French field experience with buprenorphine. *American Journal on Addictions, 13*(Suppl. 1), S17–S28.

[86] Degenhardt, L., Randall, D., Hall, W., Law, M., Butler, T., & Burns, L. (2009). Mortality among clients of a state-wide opioid pharmacotherapy program over 20 years: Risk factors and lives saved. *Drug and Alcohol Dependence, 105*(1–2), 9–15.

[87] Gibson, A., Degenhardt, L., Mattick, R. P., Ali, R., White, J., & O'Brien, S. (2008). Exposure to opioid maintenance treatment reduces long-term mortality. *Addiction, 103*(3), 462–468.

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		supervised withdrawal	
Route of Administration	Oral	Oral, intramuscular extended-release	Sublingual, buccal, subdermal implant, subcutaneous extended release
Possible Adverse Effects	Constipation, hyperhidrosis, respiratory depression, sedation, QT prolongation, sexual dysfunction, severe hypotension including orthostatic hypotension and syncope, misuse potential, neonatal abstinence syndrome	Nausea, anxiety, insomnia, precipitated opioid 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)	Constipation, nausea, precipitated opioid withdrawal, excessive sweating, insomnia, pain, peripheral edema, respiratory depression (particularly combined with benzodiazepines or other CNS depressants), misuse potential, neonatal abstinence syndrome Implant: Nerve damage during insertion/removal, accidental overdose or misuse if extruded, local migration or protrusion Subcutaneous: Injection site itching or pain,

			death f rom intravenous injection
Regulations and Availability	Schedule II; only available at federally certified OTPs and the acute inpatient hospital setting for OUD treatment	Not a scheduled medication; not included in OTP regulations; requires prescription; office-based treatment or specialty substance use treatment programs, including OTPs	Schedule III; requires waiver to prescribe outside OTPs Implant: Prescribers must be certified in the Probuphine Risk Evaluation and Mitigation Strategy (REMS) Program. Providers who wish to insert/ remove implants are required to obtain special training and certification in the REMS Program Subcutaneous: Healthcare settings and pharmacies must be certified in the Sublocade REMS Program and only dispense the medication directly to a provider for administration

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This doesn't mean that remission and recovery occur only through medication. Some people achieve remission without OUD medication, just as some people can manage type 2 diabetes with exercise and diet alone. But just as it is inadvisable to deny people with

[90] Brezing, C., & Bisaga, A. (2015, April 30). Opioid use disorder: Update on diagnosis and treatment. *Psychiatric Times, 32*(4) 1–4.

diabetes the medication they need to help manage their illness, it is also not sound medical practice to deny people with OUD access to FDA-approved medications for their illness.

Medication for OUD should be successfully integrated with outpatient and residential treatment. Some patients may benefit from different levels of care during the course of their lives. These different levels include outpatient counseling, intensive outpatient treatment, inpatient treatment, or long-term therapeutic communities. Patients receiving treatment in these settings should have access to FDA-approved medications for OUD.

Patients treated with OUD medications can benefit from individualized psychosocial supports. These can be offered by patients' healthcare providers in the form of medication management and supportive counseling and/or by other providers offering adjunctive addiction counseling, contingency management, recovery coaching, mental health services, and other services (e.g., housing supports) that particular patients may need.

The TIP expert panel strongly recommends informing all patients with OUD about the risks and benefits of treatment of OUD with all FDA-approved medications. Alternatives to these treatments and their risks and benefits should be discussed. Patients should receive access to such medications if clinically appropriate and desired by the patients.

Expanding access to FDA-approved medications is an important public health strategy. A substantial gap exists between the number of people needing OUD treatment and the capacity to treat those individuals with OUD medication. In 2012, the gap was estimated at nearly 1 million people, with approximately 80 percent of OTPs nationally operating at 80 percent capacity or greater.[91] Blue Cross Blue Shield reported a 493 percent increase in members diagnosed with OUD from 2010 to 2016 but only a 65 percent increase in the use of medication for OUD.[92]

Improving access is crucial to closing the wide gap between the need for treatment with OUD medications and the availability of such treatment, given the strong evidence of OUD medications' effectiveness.[93]

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[91] Jones, C. M., Campopiano, M., Baldwin, G., & McCance-Katz, E. (2015). National and state treatment need and capacity for opioid agonist medication-assisted treatment. *American Journal of Public Health, 105*(8), e55–e63.

[92] Blue Cross Blue Shield. (2017). *America's opioid epidemic and its effect on the nation's commercially insured population.* Washington, DC: Blue Cross Blue Shield Association.

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Methadone

Methadone retains patients in treatment and reduces illicit opioid use more effectively than placebo, medically supervised withdrawal, or no treatment, as numerous clinical trials and meta-analyses of studies conducted in many countries show. Higher methadone doses are associated with superior outcomes.[94] [95] Given the evidence of methadone's effectiveness, WHO lists it as an essential medication.[96]

Methadone treatment has by far the largest, oldest evidence base of all treatment approaches to opioid addiction. Large multisite longitudinal studies from the world over support methadone maintenance's effectiveness. Longitudinal studies have also found that it is associated with: Reduced risk of overdose-related deaths.

- Reduced risk of HIV and hepatitis C infection.
- Lower rates of cellulitis.
- Lower rates of HIV risk behavior.
- Reduced criminal behavior.

Naltrexone

XR-NTX reduces illicit opioid use and retains patients in treatment more effectively than placebo and no medication, according to findings from randomized controlled trials.

In a two-group random assignment study of adults who were opioid dependent and involved in the justice system, all participants received brief counseling and community treatment referrals. One group received no medication, and the other group received XR-NTX. During the 6-month follow-up period, compared with the no-medication group, the group that received the medication demonstrated:

- Longer time to return to substance use (10.5 weeks versus 5.0 weeks).
- A lower rate of return to use (43 percent versus 64 percent).
- A higher percentage of negative urine screens (74 percent versus 56 percent).

There are two studies comparing XR-NTX to sublingual buprenorphine. A multisite randomized trial assigned adult residential treatment patients with OUD to either XR-NTX or buprenorphine. Patients randomly assigned to buprenorphine had significantly lower relapse rates during 24 weeks of outpatient treatment than patients assigned to XR-NTX.[45] This finding resulted from challenges in completing XR-NTX induction, such that a significant

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[96] Herget, G. (2005). Methadone and buprenorphine added to the WHO list of essential medicines. *HIV/ AIDS Policy and Law Review, 10*(3), 23–24.

proportion of patients did not actually receive XR-NTX. However, when comparing only those participants who started their assigned medication, no significant between-group differences in relapse rates were observed. Because dose induction was conducted with inpatients, findings may not be generalizable to dose induction in outpatient settings, where most patients initiate treatment. A 12-week trial among adults with opioid dependence in Norway who were opioid abstinent at the time of random assignment found that XR-NTX was as effective as buprenorphine in retaining patients in treatment and in reducing illicit opioid use.

Oral naltrexone is also available, but it has not been found to be superior to placebo or to no medication in clinical trials.[97] Nonadherence limits its use.

Buprenorphine

Buprenorphine in its sublingual form retains patients in treatment and reduces illicit opioid use more effectively than placebo. It also reduces HIV risk behaviors. A multisite randomized trial with individuals addicted to prescription opioids showed that continued buprenorphine was superior to buprenorphine dose taper in reducing illicit opioid use.[98] Another randomized trial showed that continued buprenorphine also improved treatment retention and reduced illicit prescription opioid use compared with buprenorphine dose taper.[99] Long-term studies of buprenorphine show its effectiveness outside of clinical research protocols.[100] [101] Naloxone, a short-acting opioid agonist, is also often included in the buprenorphine formulation to help prevent diversion to injected misuse. Because of the evidence of buprenorphine's effectiveness, WHO lists it as an essential medication.[102] Buprenorphine is available in "transmucosal" (i.e., sublingual or buccal) formulations.

Buprenorphine implants can be effective in stable patients. FDA approved implants (Probuphine) after a clinical trial showed them to be as effective as relatively low-dose (i.e., 8 mg or less daily) sublingual buprenorphine/naloxone (Suboxone) for patients who are

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[98] Weiss, R. D., Potter, J. S., Fiellin, D. A., Byrne, M., Connery, H. S., Dickinson, W., … Ling, W. (2011). Adjunctive counseling during brief and extended buprenorphine-naloxone treatment for prescription opioid dependence: A 2-phase randomized controlled trial. *Archives of General Psychiatry, 68*(12), 1238–1246.

[99] Fiellin, D. A., Schottenfeld, R. S., Cutter, C. J., Moore, B. A., Barry, D. T., & O'Connor, P. G. (2014). Primary care-based buprenorphine taper vs maintenance therapy for prescription opioid dependence: A randomized clinical trial. *JAMA Internal Medicine, 174*(12), 1947–1954.

[100] Fiellin, D. A., Moore, B. A., Sullivan, L. E., Becker, W. C., Pantalon, M. V., Chawarski, M. C., … Schottenfeld, R. S. (2008). Long-term treatment with buprenorphine/ naloxone in primary care: Results at 2–5 years. *American Journal on Addictions, 17*(2), 116–120.

[101] Soeffng, J. M., Martin, L. D., Fingerhood, M. I., Jasinski, D. R., & Rastegar, D. A. (2009). Buprenorphine maintenance treatment in a primary care setting: Outcomes at 1 year. *Journal of Substance Abuse Treatment, 37*(4), 426–430.

[102] Herget, G. (2005). Methadone and buprenorphine added to the WHO list of essential medicines. *HIV/ AIDS Policy and Law Review, 10*(3), 23–24.

already clinically stable. More research is needed to establish implants' effectiveness outside of research studies, but findings to date are promising.

FDA approved buprenorphine extended-release injection (Sublocade) in November 2017 to treat patients with moderate or severe OUD who have first received treatment with transmucosal buprenorphine for at least 1 week. This buprenorphine formulation is a monthly subcutaneous injection.

Cost Effectiveness and Cost Benefits

Cost-effectiveness and cost-benefit analyses can further our understanding of OUD medications' effectiveness.

Data indicate that medications for OUD are cost effective. Cost-effectiveness analyses compare the cost of different treatments with their associated outcomes (e.g., negative opioid urine tests). Such analyses have found that:

- Methadone and buprenorphine are more cost effective than OUD treatment without medication.[103]
- Counseling plus buprenorphine leads to significantly lower healthcare costs than little or no treatment among commercially insured patients with OUD.[104]
- Treatment with any of the three OUD medications this TIP covers led to lower healthcare usage and costs than treatment without medication in a study conducted in a large health plan.[105]

Relatively few cost-benefit analyses have examined addiction treatment with medication separately from addiction treatment in general. Cost-benefit studies compare a treatment's cost with its benefits. The treatment is cost beneficial if its benefits outweigh its cost. These benefits can include:

- Reduced expenditures because of decreased crime.
- Reduced expenditures related to decreases in the use of the justice system.
- Improved quality of life.
- Reduced healthcare spending.
- Greater earned income.

Methadone treatment in OTPs can reduce justice system and healthcare costs.[106] [107]

Requirements and Regulations

Following is a summary of regulations and requirements that apply to the three OUD medications. Part 3 of this TIP discusses the pharmacology and dosing of these medications.

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[103] Connock, M., Juarez-Garcia, A., Jowett, S., Frew, E., Liu, Z., Taylor, R. J., … Taylor, R. S. (2007, March). Methadone and buprenorphine for the management of opioid dependence: A systematic review and economic evaluation. *Health Technology Assessment, 11*(9), 1–171, iii–iv

[104] Lynch, F. L., McCarty, D., Mertens, J., Perrin, N. A., Green, C. A., Parthasarathy, S., … Pating, D. (2014). Costs of care for persons with opioid dependence in commercial integrated health systems. *Addiction Science and Clinical Practice, 9,* 16.

[105] Baser, O., Chalk, M., Fiellin, D. A., & Gastfriend, D. R. (2011). Cost and utilization outcomes of opioid-dependence treatments. *American Journal of Managed Care, 17*(Suppl. 8), S235–S248.

[106] Cartwright, W. S. (2000). Cost-benefit analysis of drug treatment services: Review of the literature. *Journal of Mental Health Policy and Economics, 3*(1), 11–26.

[107] McCollister, K. E., & French, M. T. (2003). The relative contribution of outcome domains in the total economic benefit of addiction interventions: A review of first findings. *Addiction, 98*(12), 1647–1659.

Only federally certified and accredited OTPs can dispense methadone for the treatment of OUD. Methadone is typically given orally as a liquid.

OTPs can dispense buprenorphine under OTP regulations without using a federal waiver.

Individual healthcare practitioners can prescribe buprenorphine in any medical setting, as long as they apply for and receive waivers of the special registration requirements defined in the Controlled Substances Act by meeting the requirements of the Drug Addiction Treatment Act of 2000 (DATA 2000) and the revised Comprehensive Addiction and Recovery Act. Physicians can learn how to obtain a waiver online (www.samhsa.gov/medication-assisted -treatment/buprenorphine-waiver-management /qualify-for-physician-waiver), as can nurse practitioners and physician assistants (www.samhsa .gov/medication-assisted-treatment/qualify-nps -pas-waivers).

- Eligible physicians, nurse practitioners, and physician assistants can treat up to 30 patients at one time in the first year of practice.
- They can apply to increase this number to 100 patients in the second year.
- After a year at the 100-patient limit, **only** physicians may apply to increase to up to 275 patients (with additional practice and reporting requirements).

Prescribing buprenorphine implants requires Probuphine REMS Program certification. Providers who wish to insert or remove implants must obtain live training and certification in the REMS Program.

Healthcare settings and pharmacies must get Sublocade REMS Program certification to dispense this medication and can only dispense it directly to healthcare providers for subcutaneous administration.

Naltrexone has no regulations beyond those that apply to any prescription pharmaceutical. Any healthcare provider with prescribing
authority, including those practicing in OTPs, can prescribe its oral formulation and administer its long-acting injectable formulation.

The Controlled Substances Act contains a few exceptions from the requirement to provide methadone through an OTP or buprenorphine through an OTP or a waivered practitioner. These include (1) administering (not prescribing) an opioid for no more than 3 days to a patient in acute opioid withdrawal while preparations are made for ongoing care and (2)

administering opioid medications in a hospital to maintain or detoxify a patient as an "incidental adjunct to medical or surgical treatment of conditions other than addiction."[108]

D. Duration of Treatment With OUD Medication

Patients can take medication for OUD on a short-term or long-term basis. However, patients who discontinue OUD medication generally return to illicit opioid use. Why is this so, even when discontinuation occurs slowly and carefully? Because the more severe form of OUD (i.e., addiction) is more than physical dependence. Addiction changes the reward circuitry of the brain, affecting cognition, emotions, and behavior. Providers and their patients should base decisions about discontinuing OUD medication on knowledge of the evidence base for the use of these medications, individualized assessments, and an individualized treatment plan they collaboratively develop and agree upon. Arbitrary time limits on the duration of treatment with OUD medication are inadvisable.

1. Maintenance Treatment

The best results occur when a patient receives medication for as long as it provides a benefit. This approach is often called "maintenance treatment." Once stabilized on OUD medication, many patients stop using illicit opioids completely. Others continue to use for some time, but less frequently and in smaller amounts, which reduces their risk of morbidity and overdose death.

OUD medication gives people the time and ability to make necessary life changes associated with long-term remission and recovery (e.g., changing the people, places, and things connected with their drug use), and to do so more safely. Maintenance treatment also minimizes cravings and withdrawal symptoms. And it lets people better manage other aspects of their life, such as parenting, attending school, or working.

2. Medication Taper

After some time, patients may want to stop opioid agonist therapy for OUD through gradually tapering doses of the medication. Their outcomes will vary based on factors such as the length of their treatment, abstinence from illicit drugs, financial and social stability, and motivation to discontinue medication. Longitudinal studies show that most patients who try to stop methadone treatment relapse during or after completing the taper.[109] For example, in a large, population-based retrospective study, only 13 percent of patients who

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[108] Drug Enforcement Administration. (n.d.). Title 21 Code of Federal Regulations. Part 1306—Prescriptions. §1306.07 Administering or dispensing of narcotic drugs. Retrieved November 22, 2017, from www .deadiversion.usdoj.gov/21cfr/cfr/1306/1306_07.htm

[109] Stimmel, B., Goldberg, J., Rotkopf, E., & Cohen, M. (1977). Ability to remain abstinent after methadone detoxifcation. *JAMA, 237,* 1216–1220.

tapered from methadone had successful outcomes (no treatment reentry, death, or opioid-related hospitalization within 18 months after taper). A clinical trial of XR-NTX versus treatment without medication also found increased risk of returning to illicit opioid use after discontinuing medication.

Adding psychosocial treatments to taper regimens may not significantly improve outcomes compared with remaining on medication. One study randomly assigned participants to methadone maintenance or to 6 months of methadone treatment with a dose taper plus intensive psychosocial treatment. The maintenance group had more days in treatment and lower rates of heroin use and HIV risk behavior at 12-month follow-up.[110] Patients wishing to taper their opioid agonist medication should be offered psychosocial and recovery support services. They should be monitored during and after dose taper, offered XR-NTX, and encouraged to resume treatment with medication quickly if they return to opioid use.

3. Medically Supervised Withdrawal

Medically supervised withdrawal is a process in which providers offer methadone or buprenorphine on a short-term basis to reduce physical withdrawal signs and symptoms. Formerly called detoxification, this process gradually decreases the dose until the medication is discontinued, typically over a period of days or weeks. Studies show that most patients with OUD who undergo medically supervised withdrawal will start using opioids again and won't continue in recommended care. Psychosocial treatment strategies, such as contingency management, can reduce dropout from medically supervised withdrawal, opioid use during withdrawal, and opioid use following completion of withdrawal. Medically supervised withdrawal is necessary for patients starting naltrexone, which requires at least 7 days without short-acting opioids and 10 to 14 days without long-acting opioids. Patients who complete medically supervised withdrawal are at risk of opioid overdose.

E. Treatment Settings

Almost all healthcare settings are appropriate for screening and assessing for OUD and offering medication onsite or by referral. Settings that offer OUD treatment have expanded from specialty sites (certified OTPs, residential facilities, outpatient addiction treatment programs, and addiction specialist physicians' offices) to general primary care practices, health centers, emergency departments, inpatient medical and psychiatric units, jails and prisons, and other settings.

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[110] Sees, K. L., Delucchi, K. L., Masson, C., Rosen, A., Clark, H. W., Robillard, H., … Hall, S. M. (2000). Methadone maintenance vs 180-day psychosocially enriched detoxification for treatment of opioid dependence: A randomized controlled trial. *JAMA, 283*(10), 1303–1310.

OUD medications should be available to patients across all settings and at all levels of care—as a tool for remission and recovery.
Because of the strength of the science, a 2016 report from the Surgeon General[111] urged adoption of medication for OUD along with recovery supports and other behavioral health services throughout the healthcare system.

Challenges to Expanding Access to OUD Medication

Despite the urgent need for treatment throughout the United States, only about 21.5 percent of people with OUD received treatment from 2009 to 2013. The Centers for Disease Control and Prevention lists more than 200 U.S. counties as at risk for an HIV or a hepatitis C virus outbreak related to injection drug use.[112]

F. Scope of the Problem

The number of patients presenting with OUD in medical clinics, community health centers, and private practices is increasing. Healthcare professionals in these general settings are in an important position to identify, assess, and treat OUD or to refer patients for treatment. Moreover, patients who are medically and mentally stable can benefit from receiving OUD medications in integrated care settings, where they often have already established therapeutic relationships with their healthcare providers.

G. Screening

Screening can identify patients who may have diseases or conditions related to their substance use. Health care in general medical settings routinely includes screening for common, treatable conditions such as cancer that are associated with significant morbidity and mortality. Screening for SUDs is important, as misuse of alcohol, tobacco, and other substances is common among patients in medical settings.

Screening can identify substance misuse in patients who wouldn't otherwise discuss it or connect it with the negative consequences they're experiencing. Some patients may spontaneously reveal their substance use and ask for help. This is more likely when they're experiencing harmful consequences of substance use. However, screening may identify unhealthy substance use (e.g., binge drinking) and SUDs before patients connect their

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[111] Department of Health and Human Services, Office of the Surgeon General. (2016). *Facing addiction in America: The Surgeon General's report on alcohol, drugs, and health.* Washington, DC: Department of Health and Human Services.
[112] Van Handel, M. M., Rose, C. E., Hallisey, E. J., Kolling, J. L., Zibbell, J. E., Lewis, B., … Brooks, J. T. (2016). County-level vulnerability assessment for rapid dissemination of HIV or HCV infections among persons who inject drugs, United States. *Journal of Acquired Immune Deficiency Syndromes, 73*(3), 323–331.

substance use with their presenting complaint. Screening is also helpful when patients feel ashamed or afraid to reveal their concerns spontaneously.

Every medical practice should determine which screening tools to use and when, how, and by whom they will be administered.

Each practice should also identify steps to take when a patient screens positive. One efficient workflow strategy is to have clinical assistants or nurses administer the screening instrument in an interview or provide patients with a paper or computer tablet version for self-administration. (Self-administration is generally as reliable as interviewer administration.) Providers should be nonjudgmental and rely on established rapport when discussing screening results with patients.

Alcohol Screening

Screening for alcohol misuse can identify patients at increased risk for opioid use.

When screening patients for opioid misuse, providers should also screen for alcohol misuse and alcohol use disorder (AUD), which cause considerable morbidity and mortality. Providers should warn patients who use opioids that alcohol may increase opioid overdose risk.[113] The U.S. Preventive Services Task Force (USPSTF) recommends screening adults for alcohol misuse, including risky drinking and AUD. USPSTF also recommends brief counseling for patients with risky drinking.

The TIP expert panel recommends that healthcare professionals screen patients for alcohol, tobacco, prescription drug, and illicit drug use at least annually.

Tobacco Screening

More than 80 percent of patients who are opioid dependent smoke cigarettes.[114]

Understanding of the major health consequences and risks associated with tobacco use has grown significantly over the past 50 years. Among preventable causes of premature death, smoking remains most prevalent, with more than 480,000 deaths per year in the United States. In addition, more than 40 percent of all people who smoke are mentally ill or have SUDs.[115]

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[113] Warner-Smith, M., Darke, S., Lynskey, M., & Hall, W. (2001). Heroin overdose: Causes and consequences. *Addiction, 96*(8), 1113–1125.

[114] Kalman, D., Morissette, S. B., & George, T. P. (2005). Co-morbidity of smoking in patients with psychiatric and substance use disorders. *American Journal of Addictions, 14,* 106–123.

[115] Lasser, K., Boyd, J. W., Woolhandler, S., Himmelstein, D. U., McCormick, D., & Bor, D. H. (2000). Smoking and mental illness: A population-based prevalence study. *JAMA, 284,* 2606–2610.

USPSTF recommends that primary care providers screen for tobacco use, advise patients to quit, and provide counseling and FDA-approved medications for tobacco cessation. The six-item Fagerström Test for Nicotine Dependence assesses cigarette use and nicotine dependence. The maximum score is 10; the higher the total score, the more severe the patient's nicotine dependence. The two-item Heaviness of Smoking Index is also useful.[116]

Drug Screening

Screening for illicit drug use and prescription medication misuse is clinically advantageous. USPSTF's position as of this writing is that insufficient evidence exists to recommend for or against routine screening for illicit drug use in primary care. However, there are clinical reasons to screen for prescription medication misuse and use of illicit substances. Identifying misuse of prescription or illegal drugs can prevent harmful drug interactions, lead to adjustments in prescribing practices, improve medical care adherence, and increase the odds of patients getting needed interventions or treatment.

Brief screening instruments for drug use can determine which patients need further assessment. Providers should reinforce healthy behaviors among patients who report "no use" and direct those who report "some use" for further screening and assessment to obtain a diagnosis.

Several brief screening instruments for drug use can help primary care practitioners identify patients who use drugs. For example, a single-item screen is available for the general public.[117] A two-item valid screener is available for use with U.S. veterans.[118]

Brief drug screens don't indicate specific types of drugs used. If providers use nonspecific screens, they need to assess further which substances patients use and to what degree.

The TIP expert panel recommends universal OUD screening. Given the high prevalence of SUDs in patients visiting primary care settings and the effectiveness of medications to treat OUD specifically, the TIP expert panel recommends screening all patients for opioid misuse.

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[116] John, U., Meyer, C., Schumann, A., Hapke, U., Rumpf, H. J., Adam, C., … Lüdemann, J. (2004). A short form of the Fagerström Test for Nicotine Dependence and the Heaviness of Smoking Index in two adult population samples. *Addictive Behaviors, 29*(6), 1207–1212.

[117] Smith, P. C., Schmidt, S. M., Allensworth-Davies, D., & Saitz, R. (2010). A single-question screening test for drug use in primary care. *Archives of Internal Medicine, 170*(13), 1155–1160.

[118] Tiet, Q. Q., Leyva, Y. E., Moos, R. H., Frayne, S. M., Osterberg, L., & Smith, B. (2015). Screen of drug use: Diagnostic accuracy of a new brief tool for primary care. *JAMA Internal Medicine, 175*(8), 1371–1377.

H. Assessment

Determine the Need for and Extent of Assessment

Assess patients for OUD if:

- They screen positive for opioid misuse.
- They disclose opioid misuse.
- Signs or symptoms of opioid misuse are present.

The extent of assessment depends on a provider's ability to treat patients directly. If a provider does not offer pharmacotherapy, the focus should be on medical assessment, making a diagnosis of OUD, and patient safety. This allows the provider to refer patients to the appropriate level of treatment. The provider can also conduct:

- Assessment and treatment for co-occurring medical conditions or mental disorders.
- 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 offers pharmacotherapy, the patient needs more comprehensive assessment, including:

- 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 (e.g., urine or oral fluid drug tests, liver function tests, hepatitis B and C tests, HIV tests).

A comprehensive assessment is intended to:

- Establish the diagnosis of OUD.
- Determine the severity of OUD.
- Identify contraindicated medications.
- Indicate other medical conditions to address during treatment.
- Identify mental and social issues to address.

Set the Stage for Successful Assessment

The medical setting should create a welcoming environment that is nonjudgmental, respectful, and empathetic. Many patients with OUD are reluctant to discuss their opioid use in medical settings. A welcoming environment can help patients feel safe disclosing facts they may find embarrassing. Motivational interviewing strategies, such as asking open-ended questions, foster successful assessment. (Refer to TIP 34, *Brief Interventions and Brief Therapies for Substance Abuse*, for more specific examples of interview questions and responses.)

Staff should explore patients' ambivalence and highlight problem areas to help them find motivations for change. Almost all patients have some ambivalence about their opioid use. They will find some aspects pleasant and beneficial, but others problematic, painful, or destructive. By exploring that ambivalence and highlighting problem areas, providers can help patients discover their own motivations for change. *Motivational Interviewing: Helping People Change*[119] discusses specific applications of motivational interviewing in health care.

Take a Complete History

Staff should prioritize medical, mental health, substance use, and SUD treatment histories. When obtaining patient histories, staff should address these domains before starting treatment. As providers and staff build trust over future visits, they can get into more detailed elements of the assessment.

Medical history

Taking a complete medical history of patients with OUD is critical, as it is for patients with any other medical condition treatable with pharmacotherapy. Asking about patients' medical/ surgical history can:

- Reveal medical effects of substance use (e.g., endocarditis, soft tissue infection, hepatitis B or C, HIV infection) that may need treatment.
- Highlight consequences that motivate change.
- Identify medical issues (e.g., severe liver disease) that contraindicate or alter dosing approaches for OUD pharmacotherapies.
- Reveal chronic pain issues.
- Help providers consider interactions among various medications and other substances.

Mental health history

Assessing for comorbid mental illness is critical. Mental illness is prevalent among people with SUDs; it can complicate their treatment and worsen their prognosis. In one study, nearly

[119] Miller, W. R., & Rollnick, S. (2013). *Motivational interviewing: Helping people change* (3rd ed.). New York, NY: Guilford Press.

20 percent of primary care patients with OUD had major depression.[120] SUDs can also mimic or induce depression and anxiety disorders. Although substance-induced depression and anxiety disorders may improve with abstinence, they may still require treatment in their own right after a period of careful observation. Take a history of the relationship between a patient's psychiatric symptoms and periods of substance use and abstinence. Treatment for mental disorders and SUDs can occur concurrently.

Substance use history

Substance use histories can help gauge OUD severity, inform treatment planning, clarify potential drug interactions, and highlight the negative consequences of patients' opioid use. To help determine the severity of patients' substance use, explore historical features of their use, like:

- Age at first use.
- Routes of ingestion (e.g., injection).
- History of tolerance, withdrawal, drug mixing, and overdose.

Histories should also explore current patterns of use, which inform treatment planning and include:

- Which drugs patients use.

Open-ended, thought-provoking questions encourage patients to explore their own experiences. Ask questions like "In what ways has oxycodone affected your life?" or "What could you do to prevent infections like this in the future?" Closed-ended questions with yes/no answers—like "Has oxycodone caused your family trouble?"—can seem judgmental to patients who already feel ashamed and defensive. Closed-ended questions don't help patients become aware of and express their own circumstances and motivations, nor do they encourage patients to identify what they see as the consequences of their substance use.

Understanding patients' motivations for change can be more useful than assessing "readiness" for change. Patients coerced into treatment—such as through parole and probation or drug courts—are as likely to succeed in treatment as patients engaging voluntarily. Readiness fluctuates and depends on context. Helping patients explore why

[120] Savant, J. D., Barry, D. T., Cutter, C. J., Joy, M. T., Dinh, A., Schottenfeld, R. S., & Fiellin, D. A. (2013). Prevalence of mood and substance use disorders among patients seeking primary care office-based buprenorphine/naloxone treatment. *Drug and Alcohol Dependence, 127*(1–3), 243–247.

they want to change their drug use can motivate them and prepare their providers to support them during assessment and treatment.

Social history

Information about a patient's social environments and relationships can aid treatment planning. Social factors that may influence treatment engagement and retention, guide treatment planning, and affect prognosis include:

- Transportation and child care needs.
- Adequacy and stability of housing.
- Criminal justice involvement.
- Employment status and quality of work environment.
- Close/ongoing relationships with people with SUDs.
- Details about drug use from people the patient lives or spends time with (obtained with patient's consent).
- Sexual orientation, identity, and history, including risk factors for HIV/sexually transmitted infections.
- Safety of the home environment. Substance misuse substantially increases the risk of intimate partner violence; screen all women presenting for treatment for domestic violence.

Family history

Learn the substance use histories of patients' parents, siblings, partners, and children. One of the strongest risk factors for developing SUDs is having a parent with an SUD. Genetic factors, exposure to substance use in the household during childhood, or both can contribute to the development of SUDs.

Conduct a Physical Examination

Perform a physical exam as soon as possible if recent exam records aren't accessible. Assess for:

- Opioid intoxication or withdrawal.
- Physical signs of opioid use.
- Medical consequences of opioid use.

PATIENT TESTIMONY

Opioid Withdrawal

"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."

Opioid withdrawal

Opioid withdrawal can be extremely uncomfortable. Symptoms are similar to experiencing gastroenteritis, severe influenza, anxiety, and dysphoria concurrently.

Severity of withdrawal can indicate a patient's level of physical dependence and can inform medication choices and dosing decisions. The duration of withdrawal depends on the specific opioid from which the patient is withdrawing and can last 1 to 4 weeks. After the initial withdrawal phase is complete, many patients experience a prolonged phase of dysphoria, craving, insomnia, and hyperalgesia that can last for weeks or months.

Assess opioid withdrawal in the physical exam by noting physical signs and symptoms
Structured measures (e.g., Clinical Opiate Withdrawal Scale [COWS]; Clinical Institute Narcotic Assessment Scale for Withdrawal Symptoms) can help standardize documentation of signs and symptoms to support diagnosis, initial management, and treatment planning.

The physical signs of opioid misuse vary depending on the route of ingestion:

- Patients who primarily smoke or sniff ("snort") opioids or take them orally often have few physical signs of use other than signs of intoxication and withdrawal. However, snorting can cause congestion and damage nasal mucosa.
- Patients who inject opioids may develop:
    - Sclerosis or scarring of the veins and needle marks, or "track marks," in the arms, legs, hands, neck, or feet (intravenous use).
    - Edema in the foot, hand, or both (common in injection use, but may occur in oral use).
    - Abscesses or cellulitis.
    - Jaundice, caput medusa, palmar erythema, spider angiomata, or an enlarged or hardened liver secondary to liver disease.
    - Heart murmur secondary to endocarditis.

Obtain Appropriate Laboratory Tests

Urine or oral fluid drug testing is useful before initiating OUD pharmacotherapy. Testing establishes a baseline of substances the patient has used so that the provider can monitor the patient's response to treatment over time. Testing for a range of commonly used substances helps confirm patient histories, facilitates discussion of recent drug use and symptoms, and aids in diagnosing and determining severity of SUDs. Drug testing is an important tool in the diagnosis and treatment of addiction. A national guideline on the use of drug testing is available from ASAM.[121]

Exhibit 2.12 Urine Drug Testing Window of Detection

DRUG	POSITIVE TEST	WINDOW OF DETECTION*	COMMENTS
Amphetamine; methamphetamine; 3,4-methylenedioxy-methamphetamine	Amphetamine	1–2 days	False positives with bupropion, chlorpromazine, desipramine, fuoxetine, labetalol, promethazine, ranitidine, pseudoephedrine, trazadone, and other common medications. Confirm unexpected positive results with the laboratory.
Barbiturates	Barbiturates	Up to 6 weeks	N/A
Benzodiazepines	Benzodiazepines	1–3 days; up to 6 weeks with heavy use of long-acting benzodiazepines	Immunoassays may not be sensitive to therapeutic doses, and most immunoassays have low sensitivity to clonazepam and lorazepam. Check with your laboratory regarding sensitivity and cutoffs. False positives with sertraline or oxaprozin.
Buprenorphine	Buprenorphine	3–4 days	Will screen negative on opiate screen. Tramadol can cause false positives. Can be tested for specifically.
Cocaine	Cocaine, benzoylecgonine	2–4 days; 10–22 days	N/A

[121] Milone, M. C. (2012). Laboratory testing for prescription opioids. *Journal of Medical Toxicology, 8*(4), 408–416

		with heavy use	
Codeine	Morphine, codeine, high-dose hydrocodone	1–2 days	Will screen positive on opiate immunoassay.
Fentanyl	Fentanyl	1–2 days	Will screen negative on opiate screen. Can be tested for specifically. May not detect all fentanyl-like substances.62
Heroin	Morphine, codeine	1–2 days	Will screen positive on opiate immunoassay. 6-monoacetylmorphine, a unique metabolite of heroin, is present in urine for about 6 hours. Can be tested for specifically to distinguish morphine from heroin, but this is rarely clinically useful.
Hydrocodone	Hydrocodone, hydromorphone	2 days	May screen negative on opiate immunoassay. Can be tested for specifically.
Hydromorphone	May not be detected	1–2 days	May screen negative on opiate immunoassay. Can be tested for specifically.
Marijuana	Tetrahydrocan-nabinol	Infrequent use of 1–3 days; chronic use of up to 30 days	False positives possible with efavirenz, ibuprofen, and pantoprazole.
Methadone	Methadone	2–11 days	Will screen negative on opiate screen. Can be tested for specifically.
Morphine	Morphine, hydromorphone	1–2 days	Will screen positive on opiate immunoassay. Ingestion of

			poppy plant/ seed may screen positive.
Oxycodone	Oxymorphone	1–1.5 days	Typically screens negative on opiate immunoassay. Can be tested for specifically.

Positive opioid tests can confirm recent use. Document recent use before starting patients on buprenorphine or methadone. Positive methadone or buprenorphine tests are expected for patients receiving these treatments.

Positive opioid tests contraindicate starting naltrexone.

Negative opioid test results require careful interpretation. A patient may test negative for opioids despite presenting with opioid withdrawal symptoms if he or she hasn't used opioids for several days. A negative opioid test in the absence of symptoms of opioid withdrawal likely indicates that the patient has little or no opioid tolerance, which is important information for assessment and treatment planning. Consider that the opioid the patient reports using may not be detected on the particular immunoassay.

Screening tests are not definitive; false positive and false negative test results are possible. Confirmatory testing should follow all unexpected positive screens. Urine drug testing will detect metabolites from many prescription opioids but miss others, so it is easy to misinterpret results in patients taking these medications. False positives are also common in amphetamine testing.

Point-of-service testing provides the opportunity to discuss results with patients immediately. However, cutoffs for positive screens are not standardized across point-of-service tests. Know the specifications of the screens used.

Other laboratory tests

Patients with OUD, particularly those who inject drugs, are at risk for liver disease and blood-borne viral infections. Pregnancy is another important consideration in determining treatment course. **Recommended laboratory tests for patients with OUD include:**

Pregnancy testing, which is important because:

- It is not advisable for patients to start naltrex-one during pregnancy.
- Pregnant women treated for active OUD typically receive buprenorphine or

methadone.

- The American College of Obstetricians and Gynecologists and a recent SAMHSA-convened expert panel on the treatment of OUD in pregnancy recommend that pregnant women with OUD receive opioid receptor agonist pharmacotherapy.
- Providers should refer pregnant women to prenatal care or, if qualified, provide it themselves.

Liver function tests (e.g., aspartate aminotransferase, alanine aminotransferase, bilirubin), which can:

- Guide medication selection and dosing.
- Rule out severe liver disease, which may contraindicate OUD medication (see Part 3 of this TIP).

Hepatitis B and C serology, which can indicate:

- Patients with positive tests (evaluate for hepatitis treatment).
- The need to administer hepatitis A and B and tetanus vaccines, if appropriate.

HIV serology, which can help identify:

- Patients who are HIV positive (evaluate for antiretroviral treatment).
- Patients who are HIV negative (evaluate for preexposure prophylaxis and targeted education).

Review the PDMP

Before initiating OUD medication, providers should check their states' PDMPs to determine whether their patients receive prescriptions for controlled substances from other healthcare professionals. Using the PDMP improves the ability to manage the risks of controlled substances and to identify potentially harmful drug interactions. Although OTPs are not permitted to report methadone treatment to PDMPs, pharmacies that dispense buprenorphine and other controlled substances do report to PDMPs. Medications that need monitoring and required frequency of updates vary by state (for more information about state PDMPs, visit www.pdmpassist.org/content /state-profiles).

Determine Diagnosis and Severity of OUD

Use DSM-5 criteria to make an OUD diagnosis

Patients who meet two or three criteria have mild OUD. Those meeting four or five criteria have moderate OUD, and those meeting six or more criteria have severe OUD.

I. Treatment Planning or Referral

Making Decisions About Treatment

Start by sharing the diagnosis with patients and hearing their feedback. Patients with OUD need to make several important treatment decisions:

- Whether to begin medication to treat OUD.
- What type of OUD medication to take.

EXHIBIT 2.13. DSM-5 Criteria for OUD[122]

A problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

1. Opioids are often taken in larger amounts or over a longer period of time than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
3. A great deal of time is spent in activities to obtain the opioid, use the opioid, or recover from its effects.
4. Craving, or a strong desire or urge to use opioids.
5. Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued opioid use despite having persistent or recurrent social or interpersonal problems caused by or exacerbated by the effects of opioids.
7. Important social, occupational, or recreational activities are given up or reduced because of opioid use.
8. Recurrent opioid use in situations in which it is physically hazardous.
9. Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that's likely to have been caused or exacerbated by the substance.
10. Tolerance,* as defined by either of the following: **a.** A need for markedly increased amounts of opioids to achieve intoxication or desired effect or **b.** A markedly diminished effect with continued use of the same amount of an opioid
11. Withdrawal,* as manifested by either of the following: **a.** The characteristic opioid withdrawal syndrome or **b.** The same—or a closely related—substance is taken to relieve or avoid withdrawal symptoms

*This criterion is not met for individuals taking opioids solely under appropriate medical supervision. Severity: mild = 2–3 symptoms; moderate = 4–5 symptoms; severe = 6 or more symptoms

[122] American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing

Offer information to patients about the various treatments for OUD and collaborate with them to make decisions about treatment plans or referrals (Exhibit 2.14). Consider discussing:

- Indications, risks, and benefits of medications and alternatives to pharmacotherapy.
- Types of settings that deliver medications (including healthcare professionals' own practice locations, if applicable).
- Availability of and accessibility to treatment (i.e., transportation).
- Alternative treatments without medication (e.g., residential treatment, which often offers medically supervised opioid withdrawal).
- Costs of treatment with OUD medication, including insurance coverage and affordability.

Give patients' expressed preferences significant weight when making decisions. Patient characteristics can't reliably predict greater likelihood of success with one approved medication or another. For detailed information on medications to treat OUD, refer to Part 3 of this TIP.

Strategies to engage patients in shared decision making include:

- Indicating to patients a desire to collaborate with them to find the best medication and treatment setting for them.
- Including family members in the treatment planning process, if possible (and only with patients' consent).
- Exploring what patients already know about treatment options and dispelling misconceptions.
- Offering information on medications and their side effects, benefits, and risks
- Informing patients of the requirements of the various treatment options (e.g., admission criteria to an OTP; frequency of visits to an OBOT or OTP).
- Offering options, giving recommendations after deliberation, and supporting patients' informed decisions.

Understanding Treatment Settings and Services

Support patient preferences for treatment settings and services. Some patients prefer to receive OUD medication via physicians' offices. Others choose outpatient treatment programs that provide opioid receptor agonist treatment for medically supervised

withdrawal (with or without naltrexone) or for ongoing opioid receptor agonist maintenance treatment. Still others may want OUD treatment in a residential program with or without pharmacotherapy.

Many patients initially form a preference for a certain treatment without knowing all the risks, benefits, and alternatives. Providers should ensure that patients understand the risks and benefits of all options. Without this understanding, patients can't give truly informed consent.

Outpatient OUD Treatment Settings

Refer patients who prefer treatment with methadone or buprenorphine via an OTP and explain that:

- They will have to visit the program from 6 to 7 times per week at first.
- Additional methadone take-home doses are possible at every 90 days of demonstrated progress in treatment.
- Buprenorphine take-home doses are not bound by the same limits as methadone.
- Counseling and drug testing are required parts of OTP treatment.
- Some programs also offer case management, peer support, medical services, mental disorder treatment, and other services.

Try to arrange OTP intake appointments for patients before they leave the office. If no immediate openings are available, consider starting buprenorphine as a bridge or alternative to the OTP.

Gauge the appropriate intensity level for patients seeking non-OTP outpatient treatment for OUD. These programs range from low intensity (individual or group counseling once to a few times a week) to high intensity (2 or more hours a day of individual and group counseling several days a week). Appropriate treatment intensity depends on each patient's:

- Social circumstances.
- Severity of addiction.
- Personal preferences.
- Psychiatric/psychological needs.
- Ability to afford treatment at a given intensity.

Outpatient medical settings

Healthcare professionals cannot provide methadone in their clinics. Only those with a buprenorphine waiver can provide buprenorphine. Any healthcare professional with a license can provide naltrexone.

Once providers obtain the necessary waiver, they should offer buprenorphine treatment to all patients who present with OUD if such treatment is available and appropriate. Referring them to treatment elsewhere will likely result in delay or lack of patient access to care. Develop a treatment plan to determine where patients will receive continuing care (see the "Treatment Planning" section). Continue to provide naltrexone for patients who were already receiving it from some other setting (e.g., a prison, a specialty addiction treatment program) or for patients who meet opioid abstinence requirements and wish to take a medication for relapse prevention.

Residential drug treatment settings

Patients who have OUD, concurrent other substance use problems, unstable living situations, or a combination of the three may be appropriate candidates for residential treatment, which can last from a week to several weeks or more. Inform patients about the services and requirements typical of this treatment setting.

Some patients taking buprenorphine (or methadone) who have other SUDs, such as AUD or cocaine use disorder, can benefit from residential treatment. If such treatment is indicated, determine whether the residential program allows patients to continue their opioid receptor agonist medication while in treatment. Some residential programs require patients to discontinue these medications to receive residential treatment, which could destabilize patients and result in opioid overdose.

Residential treatment programs typically provide:

- Room and board.
- Recovery support.
- Counseling.
- Case management.
- Medically supervised withdrawal (in some programs).
- Starting buprenorphine or naltrexone (in some programs).
- Onsite mental health services (in some cases).
- Buprenorphine or methadone continuation for patients already enrolled in treatment prior to admission if their healthcare professionals have waivers or their OTP permits.

Transitioning out of residential settings requires careful planning. During a patient's stay in residential treatment, plan for his or her transition out of the program. A good transition plan maximizes the likelihood of continuity of care after discharge. Plans should also address overdose risk. Patients who are no longer opioid tolerant are at heightened risk of opioid overdose if they don't get OUD medication at discharge. Providing XR-NTX, buprenorphine, or methadone during treatment and continuing the medication after discharge can help prevent return to opioid use after discharge. Providing a naloxone prescription and overdose prevention information is appropriate.

Resource Alert

Maintaining Confidentiality

Providers who treat patients with addiction must know substance use-related disclosure rules and confidentiality requirements. SAMHSA's webpage lists frequently asked questions on substance use confidentiality and summarizes federal regulations about disclosure and patient records that federal programs maintain on addiction treatment (https://www.samhsa.gov /about-us/who-we-are/laws-regulations/confidentiality-regulations-faqs).

Key points include:

- Confidentiality regulations prohibit specialty SUD treatment programs from sharing information with healthcare professionals about patients' SUD treatment without specific consent from patients.
- Referrals to other behavioral health services require consent for sharing information on treatment progress.
- Healthcare professionals should discuss confidentiality and consent with patients during the referral process.
- OUD pharmacotherapy prescribers may consider requiring patient consent for communicating with treatment programs as a condition of receiving OUD treatment.

Treatment program staff members can help identify returns to substance use, or risk of such, before the prescriber and can work with the prescriber to stabilize patients.

Determining OUD Service Intensity and Ensuring Follow-Through

Use ASAM placement criteria for guidance on selecting the right level of OUD treatment. ASAM criteria define the level of care and key features that may make a given level (e.g., residential, intensive outpatient, standard outpatient) appropriate for a patient[79] (see the "Treatment Planning" section). To help patients select programs, note that some focus on

specific populations (e.g., gender-specific programs; parents with children; lesbian, gay, bisexual, transgender, and questioning populations).

Make an appointment with the referral program during the patient's visit rather than giving the patient a phone number to call. Follow up with the patient later to determine whether he or she kept the appointment. Doing so increases the chances of a successful referral.

Referring patients to behavioral health and support services

Discuss patients' potential need for behavioral health, peer support, and other ancillary services, like:

- Drug and alcohol counseling.
- Mental health services.
- Case management.
- Mutual-help groups.
- Peer recovery support services.

Offer referrals to counseling and tailored psychosocial support to patients receiving OUD medication.

Drug Addiction Treatment Act of 2000 legislation requires that buprenorphine prescribers be able to refer patients to counseling, but making referrals is not mandatory.[123] Many patients benefit from referral to mental health services or specialized addiction counseling and recovery support services. However, four randomized trials found no extra benefit to adding adjunctive counseling to well-conducted medical management visits delivered by the buprenorphine prescriber. There is evidence of benefits to adding contingency management to pharmacotherapy.

RESOURCE ALERT

Mutual-Support Groups

For an introduction to mutual-support groups, see SAMHSA's *Substance Abuse in Brief,* "An Introduction to Mutual Support Groups for Alcohol and Drug Abuse" (https://store.samhsa.gov/shin/content/SMA08-4336/SMA08-4336.pdf).

Make referrals to mutual-help groups.

[123] American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing

Patients may wish to participate in mutual-help groups (e.g., Alcoholics Anonymous, Narcotics Anonymous, Methadone Anonymous, Medication-Assisted Recovery Services, SMART Recovery) in addition to or instead of specialized treatment. These programs can be highly supportive, but they may pressure patients to stop taking OUD medication. If possible, refer patients to groups that welcome patients who take OUD medication.

Make referrals to medical and mental health services. Respectful, consistent medical care can support patients' efforts to recover from OUD and all other SUDs. As for any patient, providers should make appropriate referrals for patients with OUD to receive medical or mental health services beyond the providers' own scope of practice.

Patients with depression, anxiety disorders, and other mental disorders may be more likely to succeed in addiction treatment if those conditions are managed. If the severity or type of a patient's psychiatric comorbidity is beyond a provider's scope of practice, the provider should refer the patient to mental health services as appropriate.

Make referrals to ancillary services. Besides medical care and mental health services, OUD patients, like patients with other illnesses, may need more support in some areas, including ancillary services such as:

- Case management.
- Food access.
- Vocational training.
- Housing.
- Transportation.
- Legal assistance.

Helping patients who are not ready to engage in OUD treatment

Help reluctant patients be safer and approach readiness. Patients may seem unwilling to discuss their drug use if they're ashamed or fear being judged. Accepting, nonjudgmental attitudes help patients overcome shame and discuss concerns honestly while also instilling hope.

Every visit is a chance to help patients begin healthy changes and move toward treatment and recovery. Patients may not be ready to change right away. Successfully quitting drug use can take many attempts. Returns to substance use, even after periods of remission, are expected parts of the recovery process.

Patients with OUD are much more likely to die than their peers, and HIV, hepatitis C, and skin and soft tissue infections are common among this population. **Help reduce these OUD-related risks by educating patients** about:

- Using new syringes.
- Avoiding syringe sharing.
- Avoiding sharing other supplies during the injection process.
- Preventing opioid overdose (see the "Preventing Opioid-Related Overdose" section).
- Obtaining overdose prevention information and resources (e.g., *SAMHSA Opioid Overdose Prevention Toolkit* [https://store .samhsa.gov/product/SAMHSA-Opioid - Overdose-Prevention-Toolkit/SMA16-4742]).
- Obtaining naloxone and instructions for its use.

Refer patients to syringe exchange sites.

Preventing Opioid-Related Overdose

Every patient who misuses opioids or has OUD should receive opioid overdose prevention education and a naloxone prescription.[124]

- Healthcare professionals should educate patients and their families about overdose risk, prevention, identification, and response. FDA has approved an autoinjectable naloxone device (Evzio) and a naloxone nasal spray (Narcan) for use by patients and others. For information about all forms of naloxone, prescribing, and patient and community education, see the *SAMHSA Opioid Overdose Prevention Toolkit* (https://store.samhsa.gov /product/SAMHSA-Opioid-Overdose-Prevention -Toolkit/SMA16-4742).

Municipalities with community-based naloxone distribution programs have seen substantial decreases in opioid overdose death rates.[125]

Many syringe exchange programs also dispense naloxone. For information and resources on prescribing naloxone for overdose prevention, including educational patient handouts and videos, see the "Opioid-Related Overdose Prevention" section.

The United States is experiencing a death epidemic related to opioid overdose. Opioids (including prescription opioids and heroin) killed more than 33,000 people in 2015, more than in any prior year. Almost half of opioid overdose deaths involve prescription opioids.

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[124] Department of Health and Human Services. (2016). *The opioid epidemic: By the numbers.* Washington, DC: Department of Health and Human Services.

[125] Centers for Disease Control and Prevention. (2017). Heroin overdose data. Retrieved November 20, 2017, from www.cdc.gov/drugoverdose/data/heroin.html

Since 2010, heroin overdose deaths have more than quadrupled.[126] Overdose deaths from illicit fentanyl have risen sharply.[127]

Overdose risk

- Using heroin (possibly mixed with illicitly manufactured fentanyl or fentanyl analogs)
- Using prescription opioids that were not prescribed
- Using prescription opioids more frequently or at higher doses than prescribed
- Using opioids after a period of abstinence or reduced use (e.g., after medically supervised withdrawal or incarceration)
- Using opioids with alcohol, benzodiazepines, or both

Overdose prevention

- Don't use opioids that were not prescribed.
- Take medications only as prescribed.
- Don't use drugs when you are alone.
- Don't use multiple substances at once.
- Have naloxone available and make sure others know where it is and how to use it.
- Use a small "test dose" if returning to opioid use after a period of abstinence, if the substance appears altered, or if it has been acquired from an unfamiliar source. Beware: This doesn't guarantee safety; illicitly manufactured fentanyl or other substances may be present in the drug, and **any use may be fatal.**

Overdose identification

- Fingernails or lips are blue or purple.
- Breathing or heartbeat is slow or stopped.
- The person is vomiting or making gurgling noises.
- The person can't be awakened or is unable to speak.

Overdose response

- Call 9-1-1.
- Administer naloxone (more than one dose may be needed to restore adequate spontaneous breathing).
- Perform rescue breathing. If certified to provide cardiopulmonary resuscitation, perform chest compressions if there is no pulse.

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[126] Centers for Disease Control and Prevention. (2017). Heroin overdose data. Retrieved November 20, 2017, from www.cdc.gov/drugoverdose/data/heroin.html

[127] Centers for Disease Control and Prevention. (2016). Increases in drug and opioid-involved overdose deaths—United States, 2010–2015. *Morbidity and Mortality Weekly Report, 65*(50–51), 1445–1452.

- Put the person in the "recovery position," on his or her side and with the mouth facing to the side to prevent aspiration of vomit, if he or she is breathing independently.
- Stay with the person until emergency services arrive. Naloxone's duration of action is 30–90 minutes. The person should be observed after this time for a return of opioid overdose symptoms.

Resources

Alcohol and Drug Use Screening

American Academy of Addiction Psychiatry: Provides Performance in Practice Clinical Modules for screening of tobacco use and AUD. www.aaap.org/education-training /cme-opportunities

NIAAA, Professional Education Materials: Provides links to screening, treatment planning, and general information for clinicians in outpatient programs. www.niaaa.nih.gov /publications/clinical-guides-and-manuals

NIDA, Medical and Health Professionals: Provides resources for providers to increase awareness of the impact of substance use on patients' health and help identify drug use early and prevent it from escalating to misuse or addiction. www.drugabuse.gov /nidamed-medical-health-professionals

Tobacco Screening

American Psychiatric Nursing Association, Tobacco & Nicotine Use Screening Tools and Assessments: Provides the Fagerström screening tools for nicotine dependence and smokeless tobacco and a screening checklist for tobacco use. www.apna.org/i4a/pages /index.cfm?pageID=6150

U.S. Department of Health and Human Services' Be Tobacco Free: Provides information for individuals struggling with nicotine addiction and links for clinicians that provide guidance on caring for patients with nicotine addiction. https://betobaccofree.hhs.gov /health-effects/nicotine-health

U.S. Department of Health and Human Services' Million Hearts Initiative: Provides templates for developing and guidance on implementing tobacco cessation programs and guidance on implementing them as part of clinical care. https://millionhearts.hhs.gov /tools-protocols/protocols.html

Centers for Disease Control and Prevention (CDC): Offers resources and information for patients and clinicians; includes a webpage with resource links for clinicians on treating tobacco dependence. www.cdc.gov/tobacco /index.htm and www.cdc.gov/tobacco/basic_information/related_links/index.htm

Buprenorphine Treatment Locator

SAMHSA, Buprenorphine Treatment Practitioner Locator: Provides a state-by-state list of providers who offer buprenorphine. www.samhsa.gov/medication-assisted -treatment/physician-program-data /treatment-physician-locator

Buprenorphine Training, Mentorship, and Waivers

SAMHSA, Buprenorphine Waiver Management: Provides information on buprenorphine waivers with links to waiver applications; explains waiver processes, requirements, and recordkeeping. www .samhsa.gov/medication-assisted-treatment /buprenorphine-waiver-management

SAMHSA, Buprenorphine Training for Physicians: Provides links to organizations that train physicians on buprenorphine treatment. www.samhsa.gov/medication -assisted-treatment/training-resources /buprenorphine-physician-training

SAMHSA, Qualify for NPs and PAs Waiver: Provides information for NPs and PAs about the buprenorphine waiver training, with links to trainings and the application process. www .samhsa.gov/medication-assisted-treatment /qualify-nps-pas-waivers

PCSS-MAT: Provides buprenorphine waiver training and mentorship for healthcare professionals (physicians, NPs, and PAs); includes updates and other resources about medication for OUD. http://pcssmat.org

Medication Treatment for OUD

SAMHSA, *Medication-Assisted Treatment of Opioid Use Disorder:* Provides a clinical pocket guide for medication treatment for OUD. https://store.samhsa.gov/shin/content /SMA16-4892PG/SMA16-4892PG.pdf

SAMHSA, MATx Mobile App to Support Medication-Assisted Treatment of OUD: Provides a mobile app to support healthcare professionals providing medication treatment for OUD. https://store.samhsa.gov/apps/mat

SAMHSA, *Advisory,* Sublingual and Transmucosal Buprenorphine for Opioid Use Disorder: Review and Update: Summarizes information on the use of buprenorphine to treat OUD. https://store .samhsa.gov/product/Advisory-Sublingual -and-Transmucosal-Buprenorphine-for -Opioid-Use-Disorder-Review-and-Update /SMA16-4938

SAMHSA, *Clinical Use of Extended-Release Injectable Naltrexone in the Treatment of Opioid Use Disorder: A Brief Guide:* Provides a brief review of the use of XR-NTX. https://store.samhsa.gov/product/Clinical -Use-of-Extended-Release-Injectable -Naltrexone-in-the-Treatment-of-Opioid -Use-Disorder-A-Brief-Guide/SMA14-4892R

ASAM, *The ASAM National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use:* Provides national practice guidelines for the use of medications to treat OUD. www.asam.org/docs/default-source/practice -support/guidelines-and-consensus-docs /asam-national-practice-guideline-supplement .pdf

Department of Veterans Affairs/ Department of Defense, *VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders:* Provides substance use disorder practice guidelines. www.healthquality.va.gov/guidelines/MH/sud /VADoDSUDCPGRevised22216.pdf

PCSS-MAT: Provides training and mentorship for healthcare professionals (physicians, NPs, and PAs) on medications for OUD treatment including buprenorphine, naltrexone, and methadone. https://pcssmat.org

Syringe Exchange

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

Opioid-Related Overdose Prevention

Prescribe To Prevent: Provides information about naloxone prescribing for overdose prevention, including educational patient handouts and videos. http://prescribeto prevent.org

SAMHSA Opioid Overdose Prevention Toolkit: Provides healthcare professionals, communities, and local governments with material to develop practices and policies to help prevent opioid-related overdoses and deaths. It addresses issues for healthcare professionals, first responders, treatment providers, and those recovering from opioid

overdose as well as their families. https:// store.samhsa.gov/product/SAMHSA -Opioid-Overdose-Prevention-Toolkit /SMA16-4742

CDC—Injury Prevention and Overdose: Provides links and tools for clinicians to help prevent opioid overdose deaths. https://www .cdc.gov/drugoverdose/prevention/index.html

NIDA, Opioid Overdose Reversal with Naloxone (Narcan, Evzio): Provides naloxone information for providers. 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: Provides a scale that measures signs and symptoms observed in patients during withdrawal. www .ncpoep.org/wp-content/uploads/2015/02 /Appendix_7_Clinical_Institute_Narcotic_Assessment_CINA_Scale_for_Withdrawal_Symptoms.pdf

Patient and Family Education on Medications To Treat OUD

SAMHSA Store: Provides patient and family educational resources about OUD and medication treatment for OUD; some resources are available in multiple languages, including Spanish. https://store.samhsa.gov Buprenorphine. https://store.samhsa.gov /product/The-Facts-about-Buprenorphine -for-Treatment-of-Opioid-Addiction /SMA15-4442
Methadone. https://store.samhsa.gov /product/What-Every-Individual-Needs-to -Know-About-Methadone-Maintenance /SMA06-4123

ASAM Resources: Provides patient and family education tools about addiction in general and OUD specifically. Patient Resources. www.asam.org /resources/patientresources
Opioid Addiction Treatment: A Guide for Patients, Families, and Friends. https:// www.asam.org/docs/default-source /publications/asam-opioid-patient-piece_-5bopt2-5d_3d.pdf

Referral and Treatment Locators

SAMHSA, OTP Directory: Provides a state-by-state directory of methadone OTPs. https:// dpt2.samhsa.gov/treatment/directory.aspx

SAMHSA, Behavioral Health Treatment Services Locator: Provides a directory of treatment facilities. https://fndtreatment .samhsa.gov

SAMHSA, Behavioral Health Treatment Services Locator—Self-Help, Peer Support, and Consumer Groups: Provides a directory for mutual-help groups. https://fndtreatment .samhsa.gov/locator/link-focSelfGP

Screening, Assessment, and Drug Testing Resources

NIDA, Screening, Assessment, and Drug Testing Resources: Provides an evidence-based screening tool chart for adolescents and adults, drug use screening tool support materials, and a clinician resource and quick reference guide for drug screening in general medical settings, including a brief version of the ASSIST-lite. www.drugabuse.gov/nidamed -medical-health-professionals/tool-resources -your-practice/additional-screening-resources

ASAM, *The ASAM Appropriate Use of Drug Testing in Clinical Addiction Medicine:* Discusses appropriate use of drug testing in identifying, diagnosing, and treating people with or at risk for SUDs. www.asam.org /quality-practice/guidelines-and-consensus -documents/drug-testing

Treatment Planning

The ASAM Criteria: Provides criteria and a comprehensive set of guidelines for placement, continued stay, and transfer/ discharge of patients with addiction and co-occurring conditions. The ASAM six-dimensional assessment tool is designed to guide treatment planning and offers a template to organize assessments and to determine level of care.[98] www.asam.org /quality-practice/guidelines-and-consensus -documents/the-asam-criteria

SAMHSA, Decisions in Recovery— Treatment for Opioid Use Disorder: Provides an online interactive tool to support people with OUD in making informed decisions about their care. https://archive.samhsa.gov /MAT-Decisions-in-Recovery An accompanying handbook is also available. https://store.samhsa.gov/product/Decisions-in -Recovery-Treatment-for-Opioid-Use -Disorders/SMA16-4993

SAMHSA, TIP 42, *Substance Abuse Treatment for Persons With Co-Occurring Disorders:* Provides comprehensive treatment guidance for individuals with co-occurring mental and substance use disorders. https:// store.samhsa.gov/shin/content//SMA13-3992 /SMA13-3992.pdf

K. Overview of Pharmacotherapy for Opioid Use Disorder

There are three FDA-approved medications used to treat OUD, including the mu-opioid receptor partial agonist buprenorphine, the mu-opioid receptor full agonist methadone, and the mu-opioid receptor antagonist naltrexone. Extended-release naltrexone (XR-NTX) is FDA approved to prevent relapse in patients who have remained opioid abstinent for sufficient time.

Discussing medications that can treat OUD with patients who have this disorder is the clinical standard of care and should cover at least:

- The proven effectiveness of methadone, naltrexone, and buprenorphine compared with placebo and with outpatient counseling without medication.
- Risks and benefits of pharmacotherapy with all three types of medication, treatment without medication, and no treatment.
- Safety and effectiveness of the medications when used appropriately.
- Pharmacologic properties, routes of administration, and where and how to access treatment with each medication

Introduction to Medications That Address OUD

1. Methadone

Methadone is the most used and most studied OUD medication in the world. The World Health Organization (WHO) considers it an essential medication.[128] Many clinical trials and meta-analyses have shown that **it effectively reduces illicit opioid use, treats OUD, and retains patients in treatment** better than placebo or no medication.

In the United States, roughly 1,500 federally certified opioid treatment programs (OTPs) offer methadone for OUD. Increasingly, they also offer buprenorphine, and some provide XR-NTX. Core OTP services include medical oversight of treatment, direct observation of dose administration, take-home dose dispensing under certain conditions, counseling, and drug testing.

Some OTPs provide other services, including mental health and primary care, HIV and hepatitis C virus care, and recovery support. Even so, significant demand remains for better integration and coordination of care among OTPs, primary care services, and mental health services to treat the range of needs common in people with OUD.[129] Coordination is

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[128] World Health Organization. (2015). *19th WHO model list of essential medicines.* Geneva, Switzerland: Author

[129] Stoller, K. B., Stephens, M. A. C., & Schorr, A. (2016). Integrated service delivery models for opioid treatment programs in an era of increasing opioid addiction, health reform, and parity. Retrieved October 16, 2017, from www.aatod.org/wp-content/uploads/2016/07 /2nd-Whitepaper-.pdf

especially important for people with co-occurring medical, mental, and substance use disorders, who need multiple services and face challenges in treatment access and adherence.

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.

2. Naltrexone

XR-NTX has demonstrated efficacy in reducing return to illicit opioid use, increasing treatment retention, and reducing opioid craving compared with placebo or no medication in randomized controlled trials. Because the injectable form was approved more recently by FDA than methadone and buprenorphine, XR-NTX has been less studied than those medications. Physicians, NPs, and PAs may prescribe or order XR-NTX for administration by qualified staff members without additional waiver requirements.

XR-NTX initiated prior to release from controlled environments (e.g., jails, prisons, residential rehabilitation programs) **may be useful in preventing return to opioid use after release.**[130] These settings are typically associated with extended periods of opioid abstinence, so maintaining abstinence for sufficient time to start naltrexone is less challenging than initiating it among outpatients in the community. Short-term pilot studies show that offering naltrexone under these circumstances can increase treatment engagement after release.

The oral formulation of naltrexone is not widely used to treat OUD because of low rates of patient acceptance and high rates of nonadherence leading to a lack of efficacy.[131] However, consideration should be given to its use in situations where adherence can be ensured, such as with observed daily dosing. Naltrexone is also FDA approved for the treatment of alcohol use disorder and therefore may be useful for patients with both OUD and alcohol use disorder.

3. Buprenorphine

Buprenorphine is effective in retaining patients in treatment and reducing illicit opioid use, as demonstrated by many clinical trials comparing buprenorphine with placebo or no

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[130] American Society of Addiction Medicine. (2015). *The ASAM national practice guideline for the use of medications in the treatment of addiction involving opioid use.* Chevy Chase, MD: Author.

[131] Sullivan, M. A., Garawi, F., Bisaga, A., Comer, S. D., Carpenter, K., Raby, W. N., … Nunes, E. V. (2007). Management of relapse in naltrexone maintenance for heroin dependence. *Drug and Alcohol Dependence, 91*(2–3), 289–292.

medication. Buprenorphine treatment is available throughout the world. WHO includes it in its list of essential medicines.[132]

Buprenorphine is a partial agonist with a ceiling effect on opioid activity. Hence, it is less likely than methadone and other full agonists to cause respiratory depression in an accidental overdose. This property contributed to the decision permitting buprenorphine to be prescribed to treat opioid dependence outside OTPs. That being said, lethal overdose with buprenorphine is possible in opioid-naïve individuals or when it is taken in combination with central nervous system depressants such as benzodiazepines or alcohol. Transmucosal buprenorphine is available by prescription through pharmacies, because the Drug Addiction Treatment Act of 2000 (DATA 2000) created an exception to the Controlled Substances Act to permit FDA schedule III, IV, and V medications approved to treat opioid dependence to be prescribed for that purpose outside OTPs. Buprenorphine, in various formulations, is the only medication to which DATA 2000 currently applies.

Qualifying physicians, NPs, and PAs can prescribe buprenorphine if they receive special training, obtain a SAMHSA waiver under DATA 2000, and get a unique Drug Enforcement Administration registration number. This has greatly increased the number and type of settings where medication for OUD is available and the number of patients in treatment. New settings include non-OTP outpatient addiction treatment programs, as well as general medical and mental health practices or clinics (office-based opioid treatment). OTPs can also provide buprenorphine.

In 2016, FDA approved buprenorphine implants (Probuphine) that last about 6 months for patients stabilized on sublingual or buccal formulations. Implants have been found to be more effective than placebo in reducing illicit opioid use among opioid-dependent patients receiving counseling. Implants are available in the same settings as other buprenorphine formulations but require waivered providers to receive specific training from the manufacturer on insertion and removal per the FDA-approved REMS (www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=IndvRemsDetails.page&REMS=356).

In 2017, FDA approved a monthly extended-release buprenorphine injectable formulation (Sublocade) for patients with moderate-to-severe OUD who had been initiated and treated with transmucosal buprenorphine for at least 7 days. The medication is for subcutaneous abdominal injection by a healthcare provider and is intended to be available for ordering and

[132] World Health Organization. (2015). *19th WHO model list of essential medicines.* Geneva, Switzerland: Author

dispensing (not by prescription to patients) in healthcare settings that receive special certifcation, pursuant to the FDA-approved REMS (www .accessdata.fda.gov/scripts/cder/rems/index .cfm?event=IndvRemsDetails.page&REMS=376).

Choosing an OUD Medication

Currently, no empirical data indicate which patients will respond better to which OUD medications. All patients considering treatment should be educated about the effectiveness, risks, and benefits of each of the three OUD medications, treatment without medication, and no treatment. Emphasize that OUD medications are safe and effective when used appropriately, and point out that these medications can help patients reduce or stop illicit opioid use and improve their health and functioning.

Tailor decisions to patients' medical, psychiatric, and substance use histories; to their preferences; and to treatment availability when deciding which medication and treatment to provide. Consider:

- Patients' prior response to a medication.
- The medication's side effect profile.
- The strength of the published data on safety and effectiveness.
- Patients' use of other substances (e.g., naltrexone is also approved for the treatment of alcohol dependence).
- Patients' occupation. For patients in safety-sensitive occupations, consider naltrexone.
- Patients' pregnancy status.*
- Patients' physical dependence on opioids. Patients not currently physically dependent on opioids who are returning to the community from a residential treatment program or incarceration should have the option of XR-NTX,[28] methadone, or buprenorphine based on which best suits their needs and circumstances (see below for special safety dosing considerations for methadone and buprenorphine in nontolerant patients).
- Patients' preferences. Respect patients' preferences for agonist versus antagonist medication. (See Part 2 of this TIP for an in-depth discussion of treatment planning.)

Comparative Effectiveness

A Cochrane review of 5 randomized clinical trials with 788 participants found that, when provided at flexible doses on an outpatient basis, methadone retained patients in treatment

longer than buprenorphine.[133] That same review found that methadone and buprenorphine equally reduced illicit opioid use based on 8 studies with urine drug testing data from 1,027 participants and 4 studies with self-reported drug use from 501 participants.

There is not yet a Cochrane review on the comparative effectiveness of XR-NTX and buprenorphine. However, in 2017, two randomized trials comparing buprenorphine to XR-NTX were published. A multisite study with 570 participants in the United States compared initiating buprenorphine versus XR-NTX at 8 inpatient treatment programs.[134] That study found that patients randomly assigned to start buprenorphine had significantly lower return-to-use rates during 24 weeks of outpatient treatment compared with those patients assigned to start XR-NTX. This finding was due to the known difficulty in successfully completing induction in the XR-NTX group. However, comparing only the subgroups of those participants who did start their assigned medication, there were no significant between-group differences in return-to-use rates. In a 12-week trial in Norway with 159 participants who were opioid abstinent at the time of random assignment, XR-NTX was found to be noninferior to buprenorphine in terms of treatment retention and illicit opioid use.[135] There is no extant literature evaluating the comparative effectiveness of methadone, XR-NTX, buprenorphine implant, or extended-release buprenorphine injection to one another.

Duration of Medication

Continued treatment with buprenorphine or methadone is associated with better outcomes than medically supervised withdrawal.[136] Continued treatment with XR-NTX is associated with better outcomes than discontinuing XR-NTX.[137] Patients should be informed of the risks and benefits of discontinuing medication. Buprenorphine or methadone can be used for medically supervised withdrawal over a period of days to weeks for patients who prefer it to ongoing opioid agonist treatment. When opioid agonist medications are unavailable, the alpha$_2$-adrenergic agonist clonidine can relieve some withdrawal symptoms, although clinical trials found it less effective.[138] Pair medically supervised withdrawal with the chance to begin XR-NTX. Discontinuing medication increases risk of return to substance use

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[133] Mattick, R. P., Breen, C., Kimber, J., & Davoli, M. (2014). Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *Cochrane Database of Systematic Reviews, 2014*(2). CD002207.

[134] Lee, J. D., Nunes, E. V., Jr., Novo, P., Bachrach, K., Bailey, G. L., Bhatt, S., … Rotrosen, J. (2018). Comparative effectiveness of extended-release naltrexone versus buprenorphine-naloxone for opioid relapse prevention (X:BOT): A multicenter, open-label, randomized controlled trial. *Lancet, 391*(10118), 309–318.

[135] Tanum, L., Solli, K. K., Latif, Z. E., Benth, J. Š., Opheim, A., Sharma-Haase, K., … Kunøe, N. (2017). The effectiveness of injectable extended-release naltrexone vs daily buprenorphine-naloxone for opioid dependence: A randomized clinical noninferiority trial. *JAMA Psychiatry, 74*(12), 1197–1205.

[136] Department of Veterans Affairs & Department of Defense. (2015). *VA/DoD clinical practice guideline for the management of substance use disorders.* Retrieved October 16, 2017, from www.healthquality.va.gov /guidelines/MH/sud/VADoDSUDCPGRevised22216.pdf

[137] Lee, J. D., Friedmann, P. D., Kinlock, T. W., Nunes, E. V., Boney, T. Y., Hoskinson, R. A., Jr., … O'Brien, C. P. (2016). Extended-release naltrexone to prevent opioid relapse in criminal justice offenders. *New England Journal of Medicine, 374*(13), 1232–1242.

[138] Gowing, L., Ali, R., White, J. M., & Mbewe, D. (2017). Buprenorphine for managing opioid withdrawal. *Cochrane Database of Systematic Reviews, 2017*(2). CD002025.

and overdose death. Stable patients can continue on their selected OUD medication indefinitely as long as it is beneficial.[139]
During medically supervised withdrawal, ancillary medications can treat some of the withdrawal symptoms.

Principles of OUD Pharmacotherapy

Basic Function

Several factors underlie the development of addiction involving opioids and the difficulty people have in achieving and maintaining abstinence from them. These factors include:[140]

- Short-term direct and indirect mu-opioid receptor agonist effects.
- Neuroplastic changes in the brain.
- Genetic, developmental, and environmental factors (e.g., exposure to high-risk environments, effect of stress on the hypothalamic– pituitary–adrenal axis).

Methadone, buprenorphine, and naltrexone bind to the mu-opioid receptors in the central and peripheral nervous systems, gastrointestinal tract, and vascular system. In the brain, these receptors mediate opioids' analgesic and other effects (e.g., euphoria, respiratory depression, meiosis). Through modulation of mu-opioid receptor activity in the brain, these medications exert therapeutic efficacy in treating OUD.

Intrinsic Activity

Intrinsic activity at the mu-opioid receptor varies based on whether the medication is a full agonist, partial agonist, or antagonist. The amount of intrinsic activity corresponds to the amount of opioid receptor agonist effects. **A full agonist exerts maximal effects at increasing doses. A partial agonist has a ceiling effect.** Its opioid effects increase as the dose increases, but only up to a certain point. **An antagonist binds to the opioid receptor but does not stimulate the receptor at all.** Thus, it has no intrinsic activity regardless of its dose.

Overview of Medication Indications and Dosing

Healthcare professionals should consider pharmacotherapy for all patients with OUD. Prescribers must read FDA labels (i.e., package inserts) for the medications they prescribe. They must also evaluate patients clinically to determine the safety and effectiveness of the medication and dose.

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[139] Hser, Y. I., Huang, D., Saxon, A. J., Woody, G., Moskowitz, A. L., Matthews, A. G., & Ling, W. (2017). Distinctive trajectories of opioid use over an extended follow-up of patients in a multisite trial on buprenorphine + naloxone and methadone. *Journal of Addiction Medicine, 11*(1), 63–69.
[140] Kreek, M. J., Levran, O., Reed, B., Schlussman, S. D., Zhou, Y., & Butelman, E. R. (2012). Opiate addiction and cocaine addiction: Underlying molecular neurobiology and genetics. *Journal of Clinical Investigation, 122*(10), 3387–3393.

The dosing guidance in subsequent chapters for methadone, naltrexone, and buprenorphine is for healthcare professionals in general medical and addiction treatment settings. This guidance is based on:

- A review of the literature.
- A review of national and international organizations' guidelines.
- FDA-approved medication labels.
- The TIP expert panel's recommendations.

Methadone is the most studied pharmacotherapy for opioid use disorder (OUD). Of all OUD pharmacotherapies, it is used to treat the most people throughout the world and has by far the longest track record (nearly 50 years).[141] Numerous clinical trials and meta-analyses have shown that methadone treatment is associated with significantly higher rates of treatment retention and lower rates of illicit opioid use compared with placebo and with no treatment. Other research associates methadone treatment with reduced mortality, criminal behavior, and HIV seroconversion.[142] A Cochrane meta-analysis found that, at flexible doses, methadone compared with buprenorphine retains patients in treatment significantly longer and equally reduces illicit opioid use.[143]

In the United States, OTPs can offer methadone to treat OUD, but all providers who may care for patients with OUD should be familiar with this treatment.

Formulations

There are several formulations of methadone:

- Liquid concentrate, which is the formulation most commonly used in treatment programs.
- Powder, which is dissolved in water and administered as a liquid.
- Dispersible tablets, which are scored tablets that are dissolved in water.
- Tablets, which are most commonly used outside of OTPs for analgesia.

Pharmacology

Methadone, a long-acting mu-opioid receptor full agonist, is a schedule II controlled medication. It is highly plasma–protein bound and binds to proteins within tissues throughout the body.[144] Through mu-opioid receptor binding and opioid cross-tolerance to other mu-opioid

[141] Kreek, M. J., Borg, L., Ducat, E., & Ray, B. (2010). Pharmacotherapy in the treatment of addiction: Methadone. *Journal of Addictive Diseases, 29*(2), 200–216.

[142] Degenhardt, L., Randall, D., Hall, W., Law, M., Butler, T., & Burns, L. (2009). Mortality among clients of a state-wide opioid pharmacotherapy program over 20 years: Risk factors and lives saved. *Drug and Alcohol Dependence, 105*(1–2), 9–15.

[143] Mattick, R. P., Breen, C., Kimber, J., & Davoli, M. (2014). Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *Cochrane Database of Systematic Reviews, 2014*(2). CD002207.

[144] Walsh, S. L., & Strain, E. C. (2006). Pharmacology of methadone. In E. C. Strain & M. L. Stitzer (Eds.), *The treatment of opioid dependence* (pp. 59–76). Baltimore, MD: John Hopkins University Press.

agonists, at adequate doses, **methadone reduces opioid craving and withdrawal and blunts or blocks the effects of illicit opioids.**

There is wide individual variability in methadone pharmacokinetics. The half-life of methadone can vary from 8 to 59 hours depending on the patient. The average is 24 hours.[145]

Methadone has no ceiling effect. As a full agonist, increasing doses of methadone produce maximal physiological effects at the opioid receptors. Plasma levels reach steady state in about 5 days (i.e., five half-lives). Before achievement of steady state, release from tissue reservoirs can lead to increasing serum plasma levels and toxicity, even if the daily methadone dose is not changed.

Methadone induction, thus, should begin at a low dose and increase gradually with daily monitoring over days or weeks. At stable daily doses, serum levels peak 2 to 4 hours after dosing, then slowly decrease, providing 24 hours without overmedication or withdrawal.[146]

Bioavailability

Methadone is approximately 70 to 80 percent bioavailable when patients take it orally for OUD. There is notable individual variability in bioavailability, ranging from 36 to 100 percent.[147]

The liver's CYP450 3A4 enzyme is primarily responsible for metabolizing methadone, although CYP2B6 and CYP2D6 enzymes are also involved. At the start of methadone treatment, methadone can increase CYP3A4 activity and accelerate its own metabolism in some individuals.[148]

Dosing must be individualized because methadone's bioavailability, clearance, and half-life can vary considerably among patients. Providers should check for potential drug–drug interactions and monitor patients receiving concomitant medications. Some medications (e.g., benzodiazepines, anticonvulsants, antibiotics, antiretroviral agents, some

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[145] Walsh, S. L., & Strain, E. C. (2006). Pharmacology of methadone. In E. C. Strain & M. L. Stitzer (Eds.), *The treatment of opioid dependence* (pp. 59–76). Baltimore, MD: John Hopkins University Press.

[146] Payte, J. T., & Zweben, J. E. (1998). Opioid maintenance therapies. In A. W. Graham, T. K. Schultz, & B. B. Wilford (Eds.), *Principles of addiction medicine* (pp. 557–570). Chevy Chase, MD: American Society of Addiction Medicine.

[147] Eap, C. B., Buclin, T., & Baumann, P. (2002). Interindividual variability of the clinical pharmacokinetics of methadone: Implications for the treatment of opioid dependence. *Clinical Pharmacokinetics, 41*(14), 1153–1193.

[148] Eap, C. B., Buclin, T., & Baumann, P. (2002). Interindividual variability of the clinical pharmacokinetics of methadone: Implications for the treatment of opioid dependence. *Clinical Pharmacokinetics, 41*(14), 1153–1193.

antidepressants) can induce or inhibit CYP450 enzymes, resulting in potential changes in methadone serum concentration, effectiveness, and side effect profile.

Dosing Considerations

Methadone is indicated for people meeting OTP admission criteria, which for people 18 and older are:

- Being currently "opioid-addicted"—the term the Substance Abuse and Mental Health Services Administration (SAMHSA) OTP regulations use (e.g., meeting *Diagnostic and Statistical Manual of Mental Disorders,* Fifth Edition, criteria for OUD). Not all patients meeting OUD criteria, particularly those with mild OUD, are appropriate candidates for methadone.
- Having a history of at least 1 year of opioid addiction before admission.
- Providing voluntary, written informed consent.

OTP physicians can waive the history requirement per Code of Federal Regulations (42 CFR 8.12)[149] for:

- Women who are pregnant.
- Former patients (up to 2 years after discharge).
- Patients within 6 months of release from incarceration.

For patients younger than 18, admission criteria are different. They include two documented, unsuccessful, medically supervised withdrawals or treatments without OUD medication (e.g., methadone) in a 12-month period. The parent or legal guardian must provide written informed consent.

Contraindications

Contraindications to treatment with methadone include an allergy to methadone and other instances in which opioids are contraindicated, such as acute asthma, in patients with abnormally high carbon dioxide blood levels (e.g., from pulmonary disease or sleep apnea), or paralytic ileus.

Precautions and Warnings

Respiratory depression

Methadone can cause respiratory depression, particularly during initial dosing and dose titration. The goal of methadone dosing in the first weeks of treatment (i.e., induction) is to

[149] Federal opioid treatment standards, 42 CFR § 8.12 (2015).

relieve withdrawal but avoid over sedation and respiratory depression. Patients who are older or cachectic or who have chronic obstructive pulmonary disease are more susceptible to respiratory depression and should be treated cautiously with lower doses.

Individualize dosing decisions through daily monitoring of patients' responses to treatment. Opioid tolerance cannot be accurately gauged based on patient self-reports of the type, amount, or purity of the opioids they've used or of the severity of their opioid withdrawal symptoms.

The best approach to dosing is to start low and go slow. Methadone has a relatively long half-life (24–36 hours or longer). Steady-state serum levels are generally not reached until about five half-lives. **This means that patients will not feel the full effect of the initial dose for 4 or more days** even if the daily dose is the same. Slow release of methadone from tissues causes serum levels to continue to increase until reaching steady state. Initially a dose may seem appropriate, but the third or fourth day of the same dose can lead to over sedation and even respiratory depression and death.[150]

Use a lower-than-usual starting dose in individuals with no or low opioid tolerance (5 mg to 10 mg). Increase doses slowly and with careful monitoring for patients who:

- Have not used opioids for 5 or more days (e.g., after leaving a controlled environment).
- Do not use opioids daily.
- Use weaker opioids (e.g., codeine).

Do not determine doses by analgesic equivalence dose conversion tables for patients using high doses of prescription opioids, whether by prescription or illicitly. This can lead to death owing to incomplete cross-tolerance[151] and the unique pharmacology of methadone.

Concurrent substance use disorders (SUDs) involving benzodiazepines or alcohol

Concurrent misuse of alcohol or benzodiazepines with methadone (or buprenorphine) increases respiratory depression risk. Use of alcohol and benzodiazepines (illicit and prescription) is common in patients with OUD. Managing OUD with methadone for patients with alcohol or benzodiazepine use disorders is challenging and should be undertaken with

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[150] Chou, R., Cruciani, R. A., Fiellin, D. A., Compton, P., Farrar, J. T., Haigney, M. C., … Zeltzer, L. (2014). Methadone safety: A clinical practice guideline from the American Pain Society and College on Problems of Drug Dependence, in collaboration with the Heart Rhythm Society. *Journal of Pain, 15*(4), 321–337.

[151] P., Martin, J. A., McNicholas, L., … Wilford, B. B. (2013). Safe methadone induction and stabilization: Report of an expert panel. *Journal of Addiction Medicine, 7*(6), 377–386.

care. A 2017 Food and Drug Administration (FDA) Drug Safety Communication noted that although concomitant use of buprenorphine or methadone with benzodiazepines increases the risk of an adverse reaction, including overdose death, opioid agonist treatment should not be denied to patients solely on the basis of their taking benzodiazepines, because untreated OUD can pose a greater risk of morbidity and mortality.[152] FDA advises that careful medication management by healthcare professionals can reduce risk (see www.fda.gov/downloads /Drugs/DrugSafety/UCM576377.pdf for more information).

Strategies to manage patients with concurrent alcohol or benzodiazepine use disorders include the following:

- **Obtain permission to communicate with the benzodiazepine prescriber** to confirm the reason for use, adherence to treatment, and prescriber awareness of the patient's OUD. It can also help to speak (with permission) with close family members or friends to assess the extent and impact of any alcohol or benzodiazepine misuse.
- **Ensure that patients understand the risk** of potential respiratory depression and un-intentional overdose death when combining methadone with alcohol, benzodiazepines, or other central nervous system (CNS) depressants.
- **Determine whether patients require medically supervised withdrawal or tapering from alcohol or benzodiazepines.** Patients at risk for serious alcohol or benzodiazepine withdrawal syndrome (including seizures and delirium tremens) may need inpatient medically supervised withdrawal.
- **Attempt gradual outpatient medically supervised withdrawal for benzodiaze-pines when indicated.** Some OTPs have the staffing and capacity to provide a supervised outpatient taper from benzodiazepines. This usually requires use of a long-acting benzodiazepine, management of anxiety and sleeplessness, and careful monitoring with observed dosing and toxicology screening. It may also require lower-than-usual methadone doses. Engage in outpatient medically supervised withdrawal only with patients who are physically dependent on benzodiazepines but do not inject or binge. This may only be successful in a minority of patients. Attempt the taper while continuing treatment with methadone, subject to certain conditions that promote safety and reduce risk.
- **Consider increasing counseling frequency as appropriate.**
- For more information on managing benzodiaze-pine use, see *Management of Benzodiazepines in Medication-Assisted Treatment* (http://ireta .org/wp-content/uploads/2014/12/BP_Guidelines_for_Benzodiazepines.pdf).

[152] Food and Drug Administration. (2016, March). FDA Drug Safety Communications, FDA urges caution about withholding opioid addiction medications from patients taking benzodiazepines or CNS depressant: Careful medication management can reduce risks. Retrieved January 3, 2018, from www.fda.gov/downloads/Drugs /DrugSafety/UCM576377.pdf

QTc prolongation and cardiac arrhythmia

Methadone treatment has been associated with QTc prolongation, which often occurs without clinical consequences.[153] Since 2006, methadone has had an FDA black box warning on QTc prolongation and Torsades de Pointes. QTc intervals above 500 milliseconds can increase risk for this rare ventricular arrhythmia, which can be lethal.[154] The prevalence of QTc prolongation among methadone patients is not known with certainty. It has been estimated that about 2 percent of patients in methadone treatment have QTc intervals greater than 500 milliseconds.[155] According to methadone's FDA label, most Torsades de Pointes cases occur in patients receiving methadone for pain treatment, although some cases have occurred among those in methadone maintenance. High methadone doses may be associated with prolonged QTc intervals.

Other risk factors include:

- Some medications (e.g., antidepressants, antibiotics, antifungals).
- Congenital prolonged QTc interval.
- Hypokalemia.
- Bradycardia.

There is considerable controversy about how best to screen for QTc prolongation without creating barriers to methadone treatment entry.[156] Indeed, a Cochrane review of the literature was unable to draw any conclusions about the effectiveness of QTc screening strategies in preventing cardiac morbidity or mortality among methadone patients. Notwithstanding the uncertainty about the best approach, OTPs can take steps to identify patients who may be at risk for cardiac arrhythmia. **The TIP expert panel concurs with the recommendations of other expert panels (which included cardiologists) that OTPs develop a cardiac risk management plan,[157]**to the extent possible. **OTPs should consider the following elements in crafting a cardiac risk management plan:**

- **An intake assessment of risk factors, which can include:** Family history of sudden cardiac death, arrhythmia, myocardial infarction, heart failure, prolonged QTc interval, or unexplained syncope.

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[153] Bart, G., Wyman, Z., Wang, Q., Hodges, J. S., Karim, R., & Bart, B. A. (2017). Methadone and the QTc interval: Paucity of clinically significant factors in a retrospective cohort. *Journal of Addiction Medicine, 11*(6), 489–493.

[154] Bednar, M. M., Harrigan, E. P., & Ruskin, J. N. (2002). Torsades de pointes associated with nonantiarrhythmic drugs and observations on gender and QTc. *American Journal of Cardiology, 89*(11), 1316–1319.

[155] Martin, J. A., Campbell, A., Killip, T., Kotz, M., Krantz, M. J., Kreek, M. J., … Wilford, B. B. (2011). QT interval screening in methadone maintenance treatment: Report of a SAMHSA expert panel. *Journal of Addictive Diseases, 30*(4), 283–306.

[156] Bart, G., Wyman, Z., Wang, Q., Hodges, J. S., Karim, R., & Bart, B. A. (2017). Methadone and the QTc interval: Paucity of clinically significant factors in a retrospective cohort. *Journal of Addiction Medicine, 11*(6), 489–493.

[157] Martin, J. A., Campbell, A., Killip, T., Kotz, M., Krantz, M. J., Kreek, M. J., … Wilford, B. B. (2011). QT interval screening in methadone maintenance treatment: Report of a SAMHSA expert panel. *Journal of Addictive Diseases, 30*(4), 283–306.

- Patient history of arrhythmia, myocardial infarction, heart failure, prolonged QTc interval, unexplained syncope, palpitations, or seizures.
- Current use of medications that may increase QTc interval (for a complete list, see www.crediblemeds.org/pdftemp/pdf /CompositeList.pdf; register for free for the most current list).
- Patient history of use of cocaine and methamphetamines (which can prolong the QTc interval).
- Electrolyte assessment (for hypokalemia or hypomagnesemia).
- **A risk stratification plan, which can include the following: Conduct an ECG for patients with significant risk factors** at admission; repeat within 30 days. Repeat once a year and if the patient is treated with more than 120 mg of methadone per day.
- Discuss risks and benefits of methadone with patients with QTc intervals between 450 and 500 milliseconds. Adjust modifiable risk factors to reduce their risk.
    - **Do not start methadone treatment for patients with known QTc intervals above 500 milliseconds.** If such an interval is discovered during treatment, have a risk/ benefit discussion. Strongly consider lowering the methadone dose, changing concurrent medications that prolong the QTc interval, eliminating other risk factors, and, if necessary, switching to buprenor-phine. Include follow-up ECG monitoring.

− Consider providing routine universal ECG screening if feasible, although there is insufficient evidence to formally recommend doing so.[158]

Accidental ingestion

Inform patients that accidental ingestion can be fatal for opioid-naïve individuals, particularly children. Patients should safeguard take-home methadone in a lockbox out of the reach of children.

Neonatal abstinence syndrome (NAS)

Ensure awareness among pregnant patients or patients who may become pregnant that NAS can occur in newborns of mothers treated with methadone. Women receiving methadone treatment while pregnant should talk with their healthcare provider about NAS and how to reduce it. Research has shown that the dose of opioid agonist medication is not reliably related to the severity of NAS.[159] Thus, each woman should receive the dose of medication that best manages her illness.

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[158] Chou, R., Cruciani, R. A., Fiellin, D. A., Compton, P., Farrar, J. T., Haigney, M. C., … Zeltzer, L. (2014). Methadone safety: A clinical practice guideline from the American Pain Society and College on Problems of Drug Dependence, in collaboration with the Heart Rhythm Society. *Journal of Pain, 15*(4), 321–337.

[159] Jones, H. E., Dengler, E., Garrison, A., O'Grady, K. E., Seashore, C., Horton, E., … Thorp, J. (2014). Neonatal outcomes and their relationship to maternal buprenorphine dose during pregnancy. *Drug and Alcohol Dependence, 134,* 414–417.

Misuse and diversion

Alert patients to the potential for misuse and diversion of methadone.

Physical dependence

Inform patients that they will develop physical dependence on methadone and will experience opioid withdrawal if they stop taking it.

Sedation

Caution patients that methadone may affect cognition and psychomotor performance and can have sedating effects. Urge patients to be cautious in using heavy machinery and driving until they are sure that their abilities are not compromised.

Adrenal insufficiency

Adrenal insufficiency has been reported in patients treated with opioids. Ask patients to alert healthcare providers of nausea, vomiting, loss of appetite, fatigue, weakness, dizziness, or low blood pressure.[160]

Drug Interactions

Methadone has more clinically significant drug–drug interaction than buprenorphine. Carefully monitor each patient's response to treatment if they are prescribed or stop taking a CYP450 34A inducer or inhibitor. Methadone dosages may need to be adjusted up or down depending on the medication and whether treatment is starting or stopping. Exhibit 3B.2 lists common interactions between methadone and other medications.

Medications that induce CYP450 activity can increase methadone metabolism. Patients may experience craving or opioid withdrawal symptoms between doses if they begin these medications or become sedated if they discontinue them:

- Some antibiotics (e.g., rifampin).
- Antiretrovirals (e.g., efavirenz, nevirapine, ritonavir).
- Anticonvulsants (carbamazepine, phenobarbital, phenytoin).

Other medications can inhibit CYP450 activity and decrease methadone metabolism, causing symptoms of overmedication (e.g., sedation) when the medication is started and possibly withdrawal or cravings when it is stopped. Among such medications are:[117]

[160] Food and Drug Administration. (2016, March). FDA Drug Safety Communication: FDA warns about several safety issues with opioid pain medicines; requires label changes. Retrieved December 18, 2017, from www.fda .gov/downloads/Drugs/DrugSafety/UCM491302.pdf

- Some antibiotics (ciprofoxacin, erythromycin).
- Antacids (cimetidine).
- Antifungals (fuconazole).
- Antidepressants (e.g., fuvoxamine, paroxe-tine, sertraline).

Methadone can affect the metabolism of other medications. For example, zidovudine levels are reported to increase significantly during methadone treatment. Monitoring for zidovudine side effects during treatment is warranted.[119] Check drug–drug interactions online (www .drugs.com/drug_interactions.php).

Side Effects

Possible side effects of methadone include the following (methadone FDA labels list all potential side effects and are available at https://dailymed.nlm.nih.gov/dailymed/search .cfm?labeltype=all&query=METHADONE:

- Constipation
- Nausea
- Sweating
- Sexual dysfunction or decreased libido
- Drowsiness
- Amenorrhea
- Weight gain
- Edema

L. Partnering Addiction Treatment Counselors With Clients and Healthcare Professionals

Overview and Context

Scope of the Problem

Opioid misuse has caused a growing nationwide epidemic of OUD and unintentional overdose deaths.[161] This epidemic affects people in all regions, of all ages, and from all walks of life. Opioid misuse devastates families, burdens emergency departments and first responders, fuels increases in hospital admissions, and strains criminal justice and child welfare systems.

Counselors can play an integral role in addressing this crisis. Counseling helps people with OUD and other substance use disorders (SUDs) change how they think, cope, react, and

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[161] Centers for Disease Control and Prevention. (2016). Increases in drug and opioid-involved overdose deaths—United States, 2010–2015. *Morbidity and Mortality Weekly Report, 65*(50–51),1445–1452.

acquire the skills and confidence necessary for recovery. Counseling can provide support for people who take medication to treat their OUD. Patients may get counseling from prescribers or other staff members in the prescribers' practices or by referral to counselors at specialty addiction treatment programs or in private practice. Counselors and peer recovery support specialists can work with patients who take OUD medication and refer patients with active OUD to healthcare professionals for an assessment for treatment with medication.

[This section] uses "counselor" to refer to the range of professionals—including recovery coaches and other peer recovery support services specialists —who may counsel, coach, or mentor people who take OUD medication, although their titles, credentials, and range of responsibilities vary. At times, [This section] refers to individuals as "clients."

Counseling clients who take OUD medication requires understanding:

- Basic information about OUD.
- The role and function of OUD medications.
- Ways to create a supportive environment that helps clients work toward recovery.
- Counseling's role within a system of whole-person, recovery-oriented OUD care.

Setting the Stage

Since the 1990s, dramatic increases in controlled medication prescriptions—particularly opioid pain relievers—have coincided with increases in their misuse.[162] Since the mid-2000s, heroin and fentanyl (mainly illicit formulations)[163] consumption has also sharply increased. People who turn to illicit drugs after misusing opioid medications have driven greater use of heroin and fentanyl, which are cheaper and easier to obtain.

Approximately 1,500 OTPs currently dispense methadone, buprenorphine, or both.[164] They may also offer naltrexone. Historically, OTPs were the only source of OUD medication and offered only methadone.

Buprenorphine is increasingly available in general medical settings. Physicians, nurse practitioners, and physician assistants (whether or not they're addiction specialists) can get a

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[162] 10 Manchikanti, L. (2007). National drug control policy and prescription drug abuse: Facts and fallacies. *Pain Physician, 10,* 399–424.

[163] Centers for Disease Control and Prevention. (2016). Increases in drug and opioid-involved overdose deaths—United States, 2010–2015. *Morbidity and Mortality Weekly Report, 65*(50–51),1445–1452.

[164] Substance Abuse and Mental Health Services Administration. (n.d.). Opioid treatment program directory. Retrieved October 19, 2017, from https:// dpt2.samhsa.gov/treatment/directory.aspx

federal waiver to prescribe buprenorphine. These healthcare professionals can also prescribe and administer naltrexone, which does not require a waiver or OTP program certification.

People with OUD should have access to the medication most appropriate for them. Medication helps establish and maintain OUD remission. By controlling withdrawal and cravings and blocking the euphoric effects of illicit opioids, OUD medication helps patients stop illicit opioid use and resolve OUD's psychosocial problems. For some people, OUD medication may be lifesaving. Ideally, patients with OUD should have access to all three FDA-approved pharmacotherapies. (See the "Quick Guide to Medications" section for an overview of each medication.)

Many patients taking OUD medication benefit from counseling as part of their treatment. Counseling helps people with OUD change how they think, cope, react, and acquire the skills and confidence needed for recovery. Patients may get counseling from medication prescribers or staff members in prescribers' practices or by referral to counselors at specialty addiction treatment programs or in private practice.

Distinguishing OUD From Physical Dependence on Opioid Medications

According to DSM-5[165] OUD falls under the general category of SUDs and is marked by:

- Compulsion and craving.
- Tolerance.
- Loss of control.
- Withdrawal when use stops.
- Continued opioid use despite adverse consequences.

Properly taken, some medications cause tolerance and physical dependence. Medications for some chronic illnesses (e.g., steroids for systemic lupus erythematosus) can make the body build tolerance to the medications over time. If people abruptly stop taking medications on which they've become physically dependent, they can experience withdrawal symptoms. This can be serious, even fatal.

Physical dependence on a prescribed, properly taken opioid medication is distinct from OUD and opioid addiction. OUD is a behavioral disorder associated with loss of control of

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165 American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.

opioid use, use despite adverse consequences, reduction in functioning, and compulsion to use. The professionals who revised DSM-5 diagnostic criteria for OUD made several significant changes. Among the most notable was differentiating physical dependence from OUD:

- Tolerance or withdrawal symptoms related to FDA-approved medications appropriately prescribed and taken to treat OUD (buprenorphine, methadone) don't count toward diagnostic criteria for OUD.

If the individual is being treated with an OUD medication and meets no OUD criteria other than tolerance, withdrawal, or craving (but did meet OUD criteria in the past), he or she is considered in remission on pharmacotherapy.

Accepting this distinction is essential to working with clients taking OUD medication. One common question about patients taking medication for OUD is "Aren't they still addicted?" The new DSM-5 distinction makes the answer to this question "No, they're not still addicted." A person can require OUD medication and be physically dependent on it but still be in remission and recovery from OUD.

Understanding the Benefits of Medication for OUD Medication is an effective treatment for OUD.[166] People with OUD should be referred for an assessment for pharmacotherapy unless they decline.[167] To be supportive and effective when counseling clients who could benefit from or who take medication for OUD, know that:

- **Treatment with methadone and buprenorphine is associated with lower likelihood of overdose death compared with not taking these medications.**[168]

- **Medication helps people reduce or stop opioid misuse.**[169]

- **Patients taking FDA-approved medication used to treat OUD can join residential or outpatient treatment.** Decades of clinical experience in OTPs, which must provide counseling, suggest that patients taking OUD medication can fully participate in group

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[166] Connery, H. S. (2015). Medication-assisted treatment of opioid use disorder: Review of the evidence and future directions. *Harvard Review of Psychiatry, 23*(2), 63–75.

[167] American Society of Addiction Medicine. (2015). *The ASAM national practice guideline for the use of medications in the treatment of addiction involving opioid use.* Chevy Chase, MD: Author.

[168] Sordo, L., Barrio, G., Bravo, M. J., Indave, B. I., Degenhardt, L., Wiessing, L., ... Pastor-Barriuso, R. (2017). Mortality risk during and after opioid substitution treatment: Systematic review and meta-analysis of cohort studies. *British Medical Journal (Clinical Research Ed.), 357,* j1550.

[169] Merlo, L. J., Greene, W. M., & Pomm, R. (2011). Mandatory naltrexone treatment prevents relapse among opiate-dependent anesthesiologists returning to practice. *Journal of Addiction Medicine, 5*(4), 279–283.

and individual counseling, both cognitively and emotionally. Patients with concurrent SUDs (involving stimulants or alcohol) can benefit from residential treatment while continuing to take their OUD medication.

- **Randomized clinical trials indicate that OUD medication improves treatment retention and reduces illicit opioid use.**[170] Retention in treatment increases the opportunity to provide counseling and supportive services that can help patients stabilize their lives and maintain recovery.

- **The longer patients take medication, the less likely they are to return to opioid use,** whereas short-term medically supervised withdrawal rarely prevents return to use:[171] Conducting short-term medically supervised withdrawal may increase the risk of unintentional fatal overdose because of decreased tolerance after withdrawal completion.

  - Providing short-term medical treatment for OUD is the same as treating a heart attack without managing the underlying coronary disease.
  - Providing longer courses of medication that extend beyond withdrawal can allow patients to stabilize.
  - Getting stabilized, which may take months or even years, allows patients to focus on building and maintaining a healthy lifestyle.

- **Patients taking OUD medication can achieve long-term recovery.** People who continue to take medication can be in remission from OUD and live healthy, productive lives.[172]

Reviewing the Evidence on Counseling in Support of Medication To Treat OUD

Dedicated counseling can help clients address the challenges of extended recovery. For clients who seek a self-directed, purposeful life, counseling can help them:

- Improve problem-solving and interpersonal skills.
- Find incentives for reduced use and abstinence.
- Build a set of techniques to resist drug use.
- Replace drug use with constructive, rewarding activities.

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[170] Krupitsky, E., Nunes, E. V., Ling, W., Illeperuma, A., Gastfend, D. R., & Silverman, B. L. (2011). Injectable extended-release naltrexone for opioid dependence: A double-blind, placebo-controlled, multicentre randomized trial. *Lancet, 377*(9776), 1506–1533.

[171] Kakko, J., Svanborg, K. D., Kreek, M. J., & Heilig, M. (2003). 1-year retention and social function after buprenorphine-assisted relapse prevention treatment for heroin dependence in Sweden: A randomised, placebo-controlled trial. *Lancet, 361*(9358), 662–668.

[172] White, W. L. (2012). Medication-assisted recovery from opioid addiction: Historical and contemporary perspectives. *Journal of Addictive Diseases, 31*(3), 199–206.

Moreover, evidence shows that counseling can be a useful part of OUD treatment for people who take OUD medication. Impact studies of counseling for people with SUDs show that:

- **Motivational enhancement/interviewing is generally beneficial.** This approach helps get people into treatment. It also supports behavior change and, thus, recovery.

- **Cognitive–behavioral therapy (CBT) has demonstrated efficacy in the treatment of SUDs,** whether used alone or in combination with other strategies.[173] Clinical trials have not shown that CBT added to buprenorphine treatment with medical management is associated with significantly lower rates of illicit opioid use.[174] However, a secondary analysis of one of those trials found that CBT added to buprenorphine and medical management was associated with significantly greater reduction in any drug use among participants whose OUD was primarily linked to misuse of prescription opioids than among those whose OUD involved only heroin.[175] Thus, CBT may be helpful to those patients receiving buprenorphine treatment who have nonopioid drug use problems.

Case management helps establish the stability necessary for SUD remission.[176] Case management helps some people in SUD treatment get or sustain access to services and necessities, such as:

Food.
Shelter.
Income support.
Legal aid.
Dental services.
Transportation.
Vocational services.

Family therapy can address SUDs and various other family problems (e.g., family conflict, unemployment, conduct disorders). Several forms of family therapy are effective with

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[173] McHugh, R. K., Hearon, B. A., & Otto, M. W. (2010). Cognitive behavioral therapy for substance use disorders. *Psychiatric Clinics of North America, 33*(3), 511–525.

[174] Ling, W., Hillhouse, M., Ang, A., Jenkins, J., & Fahey, J. (2013). Comparison of behavioral treatment conditions in buprenorphine maintenance. *Addiction, 108*(10), 1788–1798

[175] Moore, B. A., Fiellin, D. A., Cutter, C. J., Biondo, F. D., Barry, D. C., Fiellin, L. E., … Schottenfeld, R. S. (2016). Cognitive behavioral therapy improves treatment outcomes for prescription opioid users in primary care buprenorphine treatment.

[176] Abbott, P. J. (2010). Case management: Ongoing evaluation of patients' needs in an opioid treatment program. *Professional Case Management, 15*(3), 145–152.

adolescents [177] and can potentially address family members' biases about use of medication for OUD.[178]

There is more research on combined methadone treatment and various psychosocial treatments (e.g., different levels of counseling, contingency management) than on buprenorphine or naltrexone treatment in office-based settings. More research is needed to identify the best interventions to use with specific medications, populations, and treatment phases in outpatient settings.[179]

Motivational intervention, case management, or both can improve likelihood of entry into medication treatment for OUD among people who inject opioids, according to a systematic review of 13 studies plus data from a prior systematic review.[180]

Clinical trials have shown no differences in outcomes for buprenorphine with medical management between participants who get adjunctive counseling and those who don't (i.e., prescriber-provided guidance focused specifically on use of the medication).

Yet those trials:
Relied on well-structured medical management sessions that may not be typical in practice.
Excluded patients with certain co-occurring disorders or factors that complicated treatment.

Benefits from counseling may depend on factors such as the number of sessions and adherence.[181]

Using a Recovery-Oriented Approach to Treating Patients With OUD

Counseling for OUD gives patients tools to manage their illness, achieve and sustain better health, and improve their quality of life. There are limits to how much medication alone can accomplish. OUD medication will improve quality of life, but many clients in addiction treatment have complex issues that may decrease quality of life, such as:

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[177] National Institute on Drug Abuse. (2012). *Principles of drug addiction treatment: A research-based guide* (3rd ed.). NIH Publication No. 12–4180. Bethesda, MD: Author.

[178] Woo, J., Bhalerao, A., Bawor, M., Bhatt, M., Dennis, B., Mouravska, N., … Samaan, Z. (2017). "Don't judge a book by its cover": A qualitative study of methadone patients' experiences of stigma. *Substance Abuse: Research and Treatment, 11,* 1–12.

[179] Dugosh, K., Abraham, A., Seymour, B., McLoyd, K., Chalk, M., & Festinger, D. (2016). A systematic review on the use of psychosocial interventions in conjunction with medications for the treatment of opioid addiction. *Journal of Addiction Medicine, 10*(2), 93–103.

[180] Roberts, J., Annett, H., & Hickman, M. (2011). A systematic review of interventions to increase the uptake of opiate substitution therapy in injecting drug users. *Journal of Public Health, 33*(3), 378–384.

[181] Weiss, R. D., Griffn, M. L., Potter, J. S., Dodd, D. R., Dreifuss, J. A., Connery, H. S., & Carroll, K. M. (2014). Who benefts from additional drug counseling among prescription opioid-dependent patients receiving buprenorphine-naloxone and standard medical management? *Drug and Alcohol Dependence, 140,* 118–122.

- Other SUDs (e.g., alcohol use disorder, cannabis use disorder).
- Mental distress (i.e., high levels of symptoms) and disorders (e.g., major depressive disorder, posttraumatic stress disorder).
- Medical problems (e.g., hepatitis, diabetes).
- History of trauma.
- Poor diet, lack of physical activity, or both.
- Lack of social support.
- Unemployment.

Acknowledge many pathways to recovery

Recovery occurs via many pathways. OUD medication may play a role in the beginning, middle, or entire continuum of care.

Support clients in making their own informed decisions about treatment. Counselors don't need to agree with clients' decisions but must respect them. Educate new clients about:

- Addiction as a chronic disease influenced by genetics and environment.
- How medications for OUD work.
- What occurs during dose stabilization.
- The benefits of longer-term medication use and the risks of abruptly ending treatment.

Promote recovery for clients with OUD

Focus on addressing personal and practical problems of greatest concern to clients, which can improve their engagement in treatment. Recovery supports can sustain the progress clients made in treatment and further improve their quality of life. Addressing the full range of client needs can improve clients' quality of life and lead to better long-term recovery outcomes. A recovery-oriented approach to traditional SUD counseling may help address client needs.[182]

Increasing recovery capital supports long-term abstinence and improved quality of life, especially for clients who decide to stop medication. Clients with substantial periods of abstinence from illicit drugs identify these strategies for increasing recovery capital as helpful:

- Forging new relationships with friends/family

[182] White, W. L., & Mojer-Torres, L. (2010). *Recovery-oriented methadone maintenance.* Retrieved October 23, 2017, from www.attcnetwork.org/userfles/fle /GreatLakes/5th%20Monograph_RM_Methadone.pdf

- Obtaining support from friends, family, partners, and communities
- Using positive coping strategies
- Finding meaning or a sense of purpose in life
- Engaging in a church or in spiritual practices
- Pursuing education, employment, or both
- Engaging in new interests or activities (e.g., joining a community group, exercising)
- Building confidence in ability to maintain abstinence (i.e., increasing abstinence-related self-efficacy)
- Finding ways to help other individuals who are new to recovery

Help clients further grow recovery capital by offering or connecting them to a range of services, such as:

- Ancillary services (e.g., vocational rehabilitation, supported housing).
- Additional counseling.
- Medical services.
- Mental health services.

Provide person-centered care

Clients' confidence in their ability to stay away from illicit substances, or self-efficacy, is an important factor in successful change. In person-centered care, also known as patient-centered care:

- Clients control the amount, duration, and scope of services they receive.
- They select the professionals they work with.
- Care is holistic; it respects and responds to clients' cultural, linguistic, and socioenvironmental-mental needs.[183]
- Providers implement services that recognize patients as equal partners in planning, developing, and monitoring care to ensure that it meets each patient's unique needs.

treatment empowers clients in making decisions, such as:

- Whether to take OUD medication.
- Which medication to take.
- Which counseling and ancillary services to receive.

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[183] Substance Abuse and Mental Health Services Administration. (2016). Person- and family-centered care and peer support. Retrieved October 23, 2017, from https://www.samhsa.gov/section-223/care -coordination/person-family-centered

Fragmented healthcare services are less likely to meet the full range of patients' needs. Integrated medical and behavioral healthcare delivery provides patient-focused, comprehensive treatment that meets the wide range of symptoms and service needs that patients with OUD may have. Significant demand remains for better integrated and coordinated SUD treatment (including OTP), medical, and mental health services.m Such improvements are particularly important for the many individuals with co-occurring substance use and mental disorders who receive OUD medication. In a randomized trial of methadone patients with co-occurring mental disorders receiving onsite versus offsite mental health services, those receiving services onsite had less psychiatric distress at follow-up.[184]

Promote family and social support

Support from family and friends can be the most important factor in long-term recovery, according to many people who have achieved long-term recovery from OUD.[185] Support from intimate partners helps all clients, especially women, avoid return to opioid use. But the more people in clients' social networks who use drugs, the more likely clients are to return to use.[186]

- **Most clients are willing to invite a substance-free family member or friend to support their recovery.98**

Most have at least one nearby family member who does not use illicit drugs.[99] A client's community may provide a cultural context for their recovery and culturally specific supports that may not otherwise be available in treatment.[100]

Help clients develop and support positive relations with their families by:

- Suggesting that clients invite family and friends to aid in the recovery planning process (Exhibit 4.4).
- Emphasizing the importance of relationships with family and friends who actively support recovery.
- Supporting clients in mending broken relationships with loved ones.
- Helping clients cut ties with individuals who still use drugs or enable clients' drug use.
- Encouraging clients to build new relationships that support recovery.

Provide trauma-informed care

[184] Brooner, R. K., Kidorf, M. S., King, V. L., Peirce, J., Neufeld, K., Stoller, K., & Kolodner, K. (2013). Managing psychiatric comorbidity within versus outside of methadone treatment settings: A randomized and controlled evaluation. *Addiction, 108*(11), 1942–1951.

[185] Hser, Y. I., Evans, E., Grella, C., Ling, W., & Anglin, D. (2015). Long-term course of opioid addiction. *Harvard Review of Psychiatry, 23*(2), 76–89.

[186] Schroeder, J. R., Latkin, C. A., Hoover, D. R., Curry, A. D., Knowlton, A. R., & Celentano, D. D. (2001). Illicit drug use in one's social network and in one's neighborhood predicts individual heroin and cocaine use. *Annals of Epidemiology, 11*(6), 389–394.

Trauma-informed service requires providers to realize the significance of trauma.
According to SAMHSA, trauma-informed counselors know what trauma is and also:

- Understand how trauma can affect clients, families, and communities.
- Apply knowledge of trauma extensively and consistently in both practice and policy.
- Know ways to promote recovery from trauma.
- Recognize the signs and symptoms of trauma in clients, families, staff members, and others.
- Resist things that may retraumatize or harm clients or staff.

Incorporate trauma-informed principles of care into recovery promotion efforts, because:

- Trauma histories and trauma-related disorders may increase clients' risk for various problems, including early drop-out from treatment[187] and greater problems with pain.

- Childhood trauma is highly prevalent among people with OUD.[188]
- People often suffer multiple traumas during opioid misuse.[189]
- An intervention that integrated trauma treatment and standard care (which goes further than the trauma-informed care detailed here) had better outcomes than standard care alone in a diverse group of women treated in various settings, including an OTP.[190]

Quick Guide to Medications

This section introduces the neurochemistry and biology of OUD and the medications that treat it. Reading this section will familiarize counselors with terminology healthcare professionals may use in discussing patients who take OUD medication.

Understanding the Neurobiology of OUD

Opioid receptors are a part of the body's natural endorphin system. Endorphins are chemicals our bodies release to help reduce our experience of pain. They can also contribute to euphoric feelings like the "runner's high" that some people experience. When endorphins or opioids bind to opioid receptors, the receptors activate, causing a variety of effects.

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[187] Kumar, N., Stowe, Z. N., Han, X., & Mancino, M. J. (2016). Impact of early childhood trauma on retention and phase advancement in an outpatient buprenorphine treatment program. *American Journal on Addictions, 25*(7), 542–548.

[188] Sansone, R. A., Whitecar, P., & Wiederman, M. W. (2009). The prevalence of childhood trauma among those seeking buprenorphine treatment. *Journal of Addictive Disorders, 28*(1), 64–67.

[189] Jessell, L., Mateu-Gelabert, P., Guarino, H., Vakharia, S. P., Syckes, C., Goodbody, E., … Friedman, S. (2017). Sexual violence in the context of drug use among young adult opioid users in New York City. *Journal of Interpersonal Violence, 32*(19), 2885–2907.

[190] Amaro, H., Dai, J., Arévalo, S., Acevedo, A., Matsumoto, A., Nieves, R., & Prado, G. (2007). Effects of integrated trauma treatment on outcomes in a racially/ethnically diverse sample of women in urban community-based substance abuse treatment. *Journal of Urban Health, 84*(4), 508–522.

After taking opioids, molecules bind to and activate the brain's opioid receptors and release dopamine in a brain area called the nucleus accumbens (NAc), causing euphoria. Like opioid receptors, the NAc has a natural, healthy function. For example, when a person eats, the NAc releases dopamine to reinforce this essential behavior. The NAc is a key part of the brain's reward system.

Opioid use leads to an above-normal release of dopamine, essentially swamping the natural reward pathway and turning the brain strongly toward continued use. The brain also learns environmental cues associated with this dopamine release. It associates specific people, places, and things (e.g., music, drug paraphernalia) with the euphoria; these environmental cues then become triggers for drug use.

Intermittent opioid use causes periods of euphoria followed by periods of withdrawal. The brain's strong draw toward euphoria drives repeated and continued use. Few people with OUD reexperience the euphoria they obtained early in their opioid use, yet they continue to seek it.

Changes in brain function that result from repeated drug use cause a person who once took the drug for euphoria to seek it out of habit, then compulsion. People with OUD use opioids to stave off withdrawal. Without opioids, the person feels dysphoric and physically ill, only feeling normal by taking opioids again. At the same time, other areas of the brain begin to change:[191]

- The amygdala, which is associated with feelings of danger, fear, and anger, becomes overactive.
- The frontal cortex, which is associated with planning and self-control, becomes underactive.
- The ability to control impulses diminishes, and drug use becomes compulsive.
- The need to escape the discomfort and intensely negative emotional states of withdrawal becomes the driving force of continued use.

Even after opioid use stops, brain changes linger. A person's ability to make plans and manage impulses stays underactive. That's why return to substance use is very common even after a period of abstinence.

Medications for OUD promote emotional, psychological, and behavioral stabilization.

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[191] Volkow, N. D., Koob, G. F., & McLellan, A. T. (2016). Neurobiologic advances from the brain disease model of addiction. *New England Journal of Medicine, 374*(4), 363–371.

By acting directly on the same opioid receptors as misused opioids (**but in different ways**), medications can **stabilize** abnormal brain activity.

Learning How OUD Medications Work

Buprenorphine

Buprenorphine reduces opioid misuse, HIV risk behaviors, and risk of overdose death.[192] Buprenorphine only partially activates opioid receptors; it is a partial agonist. It binds to and activates receptors sufficiently to prevent craving and withdrawal and to block the effects of illicit opioids. Appropriate doses of buprenorphine shouldn't make patients feel euphoric, sleepy, or foggy headed.

Buprenorphine has the benefit of a ceiling effect. Its effectiveness and sedation or respiratory effects don't increase after a certain dosing level, even if more is taken. This lowers risk of overdose and misuse.[193] Groups at particular risk for buprenorphine overdose include children who accidentally ingest the medication and patients who also use CNS depressants like benzodiazepines or alcohol.[194]

Buprenorphine is available outside of OTPs, through non-OTP healthcare settings (e.g., physicians' offices, outpatient drug treatment programs). Healthcare professionals (including nurse practitioners and physician assistants, per the Comprehensive Addiction and Recovery Act of 2016) can prescribe it outside of an OTP provided they have a specific federal waiver. This is often referred to as "being waivered" to prescribe buprenorphine.

Buprenorphine can cause opioid withdrawal in patients who have recently taken a full opioid agonist (e.g., heroin, oxycodone). This occurs because buprenorphine pushes the full opioid activator molecules off the receptors and replaces them with its weaker, partially activating effect. For this reason, patients must be in opioid withdrawal when they take their first dose of buprenorphine.

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[192] Edelman, E. J., Chantarat, T., Caffrey, S., Chaudhry, A., O'Connor, P. G., Weiss, L., ... Fiellin, L. E. (2014). The impact of buprenorphine/naloxone treatment on HIV risk behaviors among HIV-infected, opioid-dependent patients. *Drug and Alcohol Dependence, 139,* 79–85.

[193] Substance Abuse and Mental Health Services Administration. (2016). Buprenorphine. Retrieved October 23, 2017, from www.samhsa.gov/medication -assisted-treatment/treatment/buprenorphine

[194] Hakkinen, M., Launiainen, T., Vuori, E., & Ojanpera, I. (2012). Benzodiazepines and alcohol are associated with cases of fatal buprenorphine poisoning. *European Journal of Clinical Pharmacology, 68*(3), 301–309.

The most common buprenorphine formulation contains naloxone to reduce misuse. Naloxone is an opioid antagonist. It blocks rather than activates receptors and lets no opioids sit on receptors to activate them. Naloxone is poorly absorbed under the tongue/against the cheek, so when taking the combined medication as directed, it has no effect. If injected, naloxone causes sudden opioid withdrawal.

Buprenorphine comes in two forms that melt on the inside of the cheek or under the tongue: films (combined with naloxone) or tablets (buprenorphine/naloxone or buprenorphine alone). For treatment of OUD, patients take the films or tablets once daily, every other day, or three times a week. Various companies manufacture these forms of the medication. Some are brand name, and some are generic. The different kinds vary in strength or number of milligrams, but they have been designed and tested to provide roughly the same amount of medication as the first approved product.

Buprenorphine is also available in a long-acting implant that specially trained healthcare professionals place under the skin (subdermal implant) and an extended-release formulation that is administered under the skin (subcutaneous injection). The implant is appropriate for patients who have been stable on low doses of the films or tablets. It lasts for 6 months and can be replaced once after 6 months. The extended-release formulation lasts for 1 month and can be repeated monthly. It is appropriate for patients who have been stabilized on the films or tablets for at least 7 days.

Healthcare professionals with waivers can prescribe buprenorphine. Physicians who take an 8-hour training and get a waiver can prescribe buprenorphine. Nurse practitioners and physician assistants are eligible to apply for waivers after 24 hours of training. Providers who wish to deliver buprenorphine implants must receive special training on how to insert and remove them.

Buprenorphine can cause side effects including constipation, headache, nausea, and insomnia. These often improve over time and can be managed with dosage adjustments or other approaches. The following sections describe how each of the OUD medications functions. Discuss questions or concerns about a patient's medication, side effects, or dosage with the patient's prescriber after getting the patient's consent.

Methadone

Methadone is highly effective. Many studies over decades of research show that it:[195]

- Increases treatment retention.
- Reduces opioid misuse.
- Reduces drug-related HIV risk behavior.
- Lowers risk of overdose death.

Methadone is slow in onset and long acting, avoiding the highs and lows of short-acting opioids. It is a full agonist. Patients who take the same appropriate dose of methadone daily as prescribed will neither feel euphoric from the medication nor experience opioid withdrawal.

Methadone is an oral medication that is taken daily under observation by a nurse or pharmacist and under the supervision of an OTP physician. Methadone is available as a liquid concentrate, a tablet, or an oral solution made from a dispersible tablet or powder.

Methadone blunts or blocks the euphoric effects of illicit opioids because it occupies the opioid receptors. This "opioid blockade" helps patients stop taking illicit opioids because they no longer feel euphoric if they use illicit opioids. When on a proper dose of methadone, patients can:

- Keep regular schedules.
- Lead productive, healthy lives.
- Meet obligations (family, social, work).

Methadone can lead to overdose death in people who use a dose that's considerably higher than usual, as methadone is a full agonist. People who don't usually take opioids or have abstained from them for a while could overdose on a fairly small amount of methadone. Thus, patients start on low doses of methadone and gradually adjust upward to identify the optimal maintenance dose level.

Patients must attend a clinic for dose administration 6 to 7 days per week during the start of treatment. Healthcare professionals can thus observe patients' response to medication and discourage diversion to others. Visit frequency can lessen after patients spend time in treatment and show evidence of progress.

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[195] Fullerton, C. A., Kim, M., Thomas, C. P., Lyman, D. R., Montejano, L. B., Dougherty, R. H., ... Delphin- Rittmon, M. E. (2014). Medication-assisted treatment with methadone: Assessing the evidence. *Psychiatric Services, 65*(2), 146–157.

Methadone can cause certain side effects.
Common potential side effects of methadone include:

- Constipation.
- Sleepiness.
- Sweating.
- Sexual dysfunction.
- Swelling of the hands and feet.

Sleepiness can be a warning sign of potential overdose. Patients who are drowsy should receive prompt medical assessment to determine the cause and appropriate steps to take—which may require a reduction in methadone dose. Some patients may appear sleepy or have trouble staying awake when idle, even if there is no immediate danger of evolving overdose. These patients may need a lower dose or may be taking other prescribed or nonprescribed medications (e.g., benzodiazepines, clonidine) that are interacting with the methadone.

Naltrexone

Naltrexone stops opioids from reaching and activating receptors, preventing any reward from use. Naltrexone is an antagonist of the opioid receptors—it does not activate them at all. Instead, it sits on the receptors and blocks other opioids from activating them.

Naltrexone appears to reduce opioid craving[196] but not opioid withdrawal (unlike buprenorphine and methadone, which reduce both craving and withdrawal). Someone starting naltrexone must be abstinent from short-acting opioids for at least 7 days and from long-acting opioids for 10 to 14 days before taking the first dose. Otherwise, it will cause opioid withdrawal, which can be more severe than that caused by reducing or stopping opioid use.

Naltrexone comes in two forms: tablet and injection.

- Patients take naltrexone tablets daily or three times per week. Tablets are rarely effective, as patients typically stop taking them after a short time.[197]

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[196] Lee, J. D., Friedmann, P. D., Kinlock, T. W., Nunes, E. V., Boney, T. Y., Hoskinson, R. A., Jr., ... O'Brien, C. P. (2016). Extended-release naltrexone to prevent opioid relapse in criminal justice offenders. *New England Journal of Medicine, 374*(13), 1232–1242.

[197] Merlo, L. J., Greene, W. M., & Pomm, R. (2011). Mandatory naltrexone treatment prevents relapse among opiate-dependent anesthesiologists returning to practice. *Journal of Addiction Medicine, 5(*4), 279–283.

- **Highly externally monitored populations in remission may do well with the tablet,**[198] such as physicians who have mandatory frequent urine drug testing and are at risk of losing their licenses.
- **The injected form is more effective than the tablet because it lasts for 1 month.** Patients can come to a clinic to receive an intramuscular injection in their buttock.

Naltrexone can produce certain side effects,
which may include:

- Nausea.
- Headache.
- Dizziness.
- Fatigue.

For the extended-release injectable formulation, potential reactions at the injection site include:

- Pain.
- Bumps.
- Blistering.
- Skin lesions (may require surgery).

Knowing What Prescribers Do
The following sections will help explain the role healthcare professionals play in providing each OUD medication as part of collaborative care.

Administer buprenorphine

Patients typically begin buprenorphine in opioid withdrawal. Patients may take their first dose in the prescriber's office so the prescriber can observe its initial effects. Increasingly often, patients take their first dose at home and follow up with prescribers by phone. Most people are stable on buprenorphine dosages between 8 mg and 24 mg each day.

Patients who take buprenorphine visit their prescriber regularly to allow monitoring of their response to treatment and side effects and to receive supportive counseling. The visits may result in specific actions, such as adjusting the dosage or making a referral for psychosocial services. Stable patients may obtain up to a 30-day prescription of this medication through community pharmacies. Visits may include urine drug testing. Early in

[198] Cornish, J. W., Metzger, D., Woody, G. E., Wilson, D., McLellan, A. T., Vandergrift, B., & O'Brien, C. (1997). Naltrexone pharmacotherapy for opioid dependent federal probationers. *Journal of Substance Abuse Treatment, 14*(6), 529–534.

treatment, patients typically see their prescribers at least weekly. Further along, they may visit prescribers every 1 to 2 weeks and then as infrequently as once a month or less.

The prescriber will make dosage adjustments as needed, reducing for side effects or increasing for unrelieved withdrawal or ongoing opioid misuse. OTPs that provide buprenorphine will typically follow a similar process, with the principal difference being that the program will administer or dispense the medication rather than the patient filling a prescription at a pharmacy.

Administer methadone

Only SAMHSA-certified OTPs may provide methadone by physician order for daily observed administration onsite or for self-administration at home by stable patients.[199] The physician will start patients on a low dose of methadone. People in early methadone treatment are required by federal regulation to visit the OTP six to seven times per week to take their medication under observation. The physician will monitor patients' initial response to the methadone and slowly increase the dose until withdrawal is completely relieved for 24 hours.

A prescriber can't predict at the start of treatment what daily methadone dose will work for a patient. An effective dose is one that eliminates withdrawal symptoms and most craving and blunts euphoria from self-administered illicit opioids without producing sedation. On average, higher dosages of methadone (60 mg to 100 mg daily) are associated with better outcomes than lower dosages.[200] That said, an effective dose of methadone for a particular patient can be above or below that range.

The prescriber will continue to monitor the patient and adjust dosage slowly up or down to find the optimum dose level. The dose may need further adjustment if the patient returns to opioid use, experiences side effects such as sedation, starts new medications that may interact with methadone, or has a change in health that causes the previously effective dose to become inadequate or too strong.

If patients taking methadone drink heavily or take sedatives (e.g., benzodiazepines), **physicians may:**

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[199] Substance Abuse and Mental Health Services Administration. (2016). *Medication-assisted treatment of opioid use disorder pocket guide.* HHS No. (SMA) 16-4892PG. Rockville, MD: Substance Abuse and Mental Health Services Administration.

[200] Faggiano, F., Vigna-Taglianti, F., Versino, E., & Lemma, P. (2003). Methadone maintenance at different dosages for opioid dependence. *Cochrane Database of Systematic Reviews, 2003*(3), 1–45.

- Treat the alcohol misuse.
- Refer to a higher level of care.
- Address comorbid anxiety or depression.
- Decrease dosage to prevent overdose.

Administer naltrexone

To avoid severe withdrawal, prescribers will ensure that patients are abstinent from opioids at least 7 to 10 days before initiating or resuming naltrexone. Prescribers may require longer periods of abstinence for patients transitioning from buprenorphine or methadone to naltrexone.

Prescribers typically take urine drug screens to confirm abstinence before giving naltrexone. Healthcare professionals can confirm abstinence through a "challenge test" with naloxone, a short-acting opioid antagonist.

Healthcare professionals manage withdrawal symptoms with nonopioid medication. Prescribers are prepared to handle withdrawal caused by naltrexone despite a period of abstinence.[201] Ideally, they administer the first injection before patients' release from residential treatment or other controlled settings (e.g., prison) so qualified individuals can monitor them for symptoms of withdrawal.

Healthcare professionals typically see patients at least monthly to give naltrexone injections. For those taking oral naltrexone, prescribers schedule visits at their discretion. Thus, urine drug testing may be less frequent for these patients than for patients taking buprenorphine. But periodic drug testing should occur.

There is only one dose level for injected naltrexone,[202] so prescribers cannot adjust the dose. However, they can slightly shorten the dosing interval if the medication's effectiveness decreases toward the end of the monthly dosing interval. If the patient is having side effects or intense cravings, the prescriber may recommend switching to a different medication.

Set expectations

[201] Substance Abuse and Mental Health Services Administration. (2015). *Clinical use of extended-release injectable naltrexone in the treatment of opioid use disorder: A brief guide.* HHS Publication No. (SMA) 14-4892R. Rockville, MD: Substance Abuse and Mental Health Services Administration.

[202] National Library of Medicine. (2015). VIVITROL – naltrexone. Retrieved October 23, 2017, from https://dailymed.nlm.nih.gov/dailymed/drugInfo .cfm?setid=cd11c435-b0f0-4bb9-ae78-60f101f3703f

Ideally, prescribers will collaborate with counselors and other care providers involved in patients' care to set reasonable patient expectations. Medications can effectively treat OUD, but they don't treat other SUDs (save naltrexone, also FDA-approved to treat alcohol use disorder). Patients may still need:

- Counseling for psychosocial issues.
- Social supports/treatment to get back on track.
- Medications, therapy, or both for co-occurring conditions.

Collaboration between all involved healthcare providers helps patients understand the OUD treatment timeline, which generally lasts months or years. Courses of medically supervised withdrawal or tapering are considerably less effective than longer term maintenance treatment with buprenorphine or methadone and are often associated with return to substance use and a heightened risk of overdose.

Patients may still benefit from the counseling you can offer in addition to care from other providers, even if you can't communicate with those providers directly.

1. Counselor–Prescriber Communications

OUD medication can support counselors' work with clients who have OUD, and counseling supports the work prescribers do with them.

Good communication facilitates mutually supportive work. A counselor will probably:

- See patients more frequently than prescribers.
- Have a more complete sense of patients' issues.
- Offer providers valuable context and perspective.
- Help patients take medications appropriately.
- Ensure that patients receive high-quality care from their other providers.

Obtaining Consent

Get written consent from patients allowing communication directly with their providers (unless the counselor and the providers work in the same treatment program). The consent must explicitly state that the patient allows the counselor to discuss substance-use-related issues. It should also specify which kinds of information the counselor can share (e.g.,

medical records, diagnoses). Consent forms must comply with federal and state confidentiality laws that govern the sharing of information about patients with SUDs.[203] **Carefully protect any identifying information about patients and their medical and treatment information.** Don't send such information through unsecured channels, such as:

- Text messaging.
- Unsecure, unencrypted emails.
- Faxes to unsecured machines.

Good communication with prescribers and other treatment team members allows everyone to work together to:

- **Assess patient progress.**
- **Change treatment plans if needed.**
- **Make informed decisions about OUD medication.**

Phone calls are the most secure way to discuss patient cases, although it may be more convenient to reach out to healthcare professionals first through email.

Structuring Communications With Prescribers

Regular, structured communication can improve the flow of information between treatment teams. Some multidisciplinary programs produce regular reports for prescribers about patient progress.

Helping Clients Overcome Challenges in Accessing Resources

By collaborating with healthcare professionals in OUD care, counselors can help clients overcome challenges they face in obtaining treatment, such as:

Ability to pay for OUD medication. Counselors are often already skilled in helping clients address treatment costs (e.g., facilitating Medicaid applications, linking them to insurance navigators). Try to refer clients who face difficulty meeting prescription costs or copays back to the agency's financial department for sliding scale adjustments and ability-to-pay assessments. Also try to help patients find and apply for relevant pharmaceutical company medication prescription plans.

[203] Confidentiality of Substance Use Disorder Patient Records. ; HHS Final Rule, 82 Fed. Reg. 6052 (January 18, 2017) (to be codified at 42 CFR pt. 2). Retrieved November 13, 2017, from https://www.federalregister .gov/documents/2017/01/18/2017-00719/confidentiality -of-substance-use-disorder-patient-records

Transportation. Options to offer clients may include: Providing vouchers for public transportation.
Providing information on other subsidized transportation options.
Linking clients to peer support specialists and case managers who can arrange transportation.
Assisting eligible clients in navigating Medicaid to obtain transportation services.
If available, arranging for telehealth services to overcome clients' transportation barriers.

Access to medication in disaster situations. Counselors can review options with patients for obtaining prescription replacements and refills or daily medicine dosing under various scenarios. This could include if their usual clinic or primary pharmacy is closed or if they're relocated without notice because of an unforeseen emergency. Also advise patients on the items to take with them in such scenarios to facilitate refills from a new medication-dispensing facility. Key materials include: Photo identification.
Medication containers of currently prescribed medications (even if empty).
Written prescriptions.
Packaging labels that contain dosage, prescriber, and refill information.
Any payment receipts that contain medication information.

To overcome systemic barriers, help enact collaborative policies and procedures. Work with program management and the community at large to address the following issues:

Connection to treatment: Counselors may be able to participate in community efforts to ensure that information on how to obtain treatment for OUD is available wherever people with OUD: Gather (e.g., all-night diners, bars, free health clinics, injection equipment exchanges).
Seek help (e.g., emergency departments, houses of worship, social service agencies).
Reveal a need for help (e.g., encounters with law enforcement and child welfare agencies).
Encourage buprenorphine prescribers to make known their availability if they are prepared to accept new patients. Help disseminate lists of addiction treatment providers and share their information via peer recovery specialists.

Rapid assessment and treatment initiation: Try to help OUD pharmacotherapy providers, particularly in OTPs, streamline counseling intake processes to help patients receive medication efficiently. The expert panel of this TIP recognizes that same-day admission of patients with OUD may not be possible in all settings, but it's a worthwhile goal. Every program should streamline its intake processes and expedite admissions.

Return to treatment: When patients discontinue treatment prematurely and return to use of opioids, it can be hard for them to reengage in treatment because of the shame they feel or because there is a waiting list for admission. The waitlist problem may not be solvable because of capacity limitations, but all collaborative care team members— including counselors and prescribers—should: Inform patients from intake onward that the program will readmit them even if they drop out.
Encourage patients to seek readmission if they return to opioid use or feel that they are at risk for returning to opioid use.

Inform patients of the importance of overdose prevention
(see the "Counseling Patients on Overdose Prevention and Treatment" section).
Provide continued monitoring if possible; it can range from informal quarterly check-ins to regularly scheduled remote counseling or peer support (e.g., from a recovery coach).
Offer an expedited reentry process to encourage patients to return if they need to.
Engage in active outreach and reengage-ment with OTP patients, which can be effective.[204]
Try to contact patients who have dropped out to encourage them to return.

2. Creation of a Supportive Counseling Experience

Maintaining the Therapeutic Alliance

The therapeutic alliance is a counselor's most powerful tool for influencing outcomes.[205]
It underlies all types and modalities of therapy and helping services. A strong alliance welcomes patients into treatment and creates a sense of safety.

COUNSELING PATIENTS WITH OUD WHO DON'T TAKE MEDICATION

Patients who don't take an OUD medication after withdrawal are at high risk of return to opioid use, which can be fatal given the loss of opioid tolerance. Provide these patients with overdose prevention education and the overdose-reversal medication naloxone, or educate them about naloxone and how they can obtain it in their community. Advise them to report a return to opioid use or a feeling that they are at risk of relapsing. Work with them and their care team to either resume medication for OUD or enter a more intensive level of behavioral care.

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[204] Coviello, D. M., Zanis, D. A., Wesnoski, S. A., & Alterman, A. I. (2006). The effectiveness of outreach case management in re-enrolling discharged methadone patients. *Drug and Alcohol Dependence, 85*(1), 56–65.
[205] Duncan, B. (2010). On becoming a better therapist. *Psychotherapy in Australia, 16*(4), 42–51.

Certain counselor skills help build and maintain a therapeutic alliance, including:

- Projecting empathy and warmth.
- Making patients feel respected and understood.
- Not allowing personal opinions, anecdotes, or feelings to influence the counseling process (unless done deliberately and with therapeutic intention).

These skills are relevant for working with all patients, including those taking medication for OUD. Apply them consistently from the very first interaction with a patient through the conclusion of services. For example, recognize and reconcile personal views about medication for OUD so that they don't influence counseling sessions.

Educating Patients About OUD and a Chronic Care Approach to Its Treatment
Help ensure that patients understand the chronic care approach to OUD and their:

- Diagnosis.
- Prognosis.
- Treatment options.
- Available recovery supports.
- Prescribed medications.
- Risk of overdose (and strategies to reduce it).

Seek to understand patients' preferences and goals. Doing so can help convey information meaningfully so patients understand the choices available to them. Also, help communicate patients' preferences and goals to healthcare professionals and family members.

Educate colleagues and other staff members so they can help create a supportive experience for patients with OUD:

- Provide basic education to colleagues about medications for OUD and how they work.
- Share evidence on how these medications reduce risky behavior, improve outcomes, and save lives.

- Note that major U.S. and international guidelines affirm use of medication to treat OUD.
- Ask about and address specific fears and concerns.
- Provide resources for additional information.

Counseling Patients on Overdose Prevention and Treatment

Know how to use naloxone to treat opioid overdose; share this information with patients and their family members and friends. Available by prescription (or without a prescription in some states), naloxone is an opioid antagonist that has successfully reversed many thousands of opioid overdoses. It comes in auto-injector and nasal spray formulations easy for laypeople to administer immediately on the scene of an overdose, before emergency responders arrive.

Ask patients if they have a naloxone prescription or help them get it without one if possible. Providers may prescribe naloxone in addition to OUD medication. Counselors should check state laws to learn their jurisdiction's naloxone prescription and dispensation policies (see "Resource Alert: Overdose Prevention/ Treatment").

Inform clients and their friends and families of any Good Samaritan laws in the jurisdiction, which protect against drug offenses for people who call for medical help while experiencing or observing overdose.

Emphasize that a person given naloxone to reverse overdose must go to the emergency department, because overdose can start again when naloxone wears off.

Consider working with the program administrator to place a naloxone rescue kit in the office, if one is not already available. To be ready for an emergency, learn:

- The signs of overmedication (which may progress to overdose) and overdose itself.
- What to do if an overdose is suspected.

- How to administer naloxone.

Consider working with the program administrators to set up a program to distribute naloxone directly to patients. Many states allow organizations to do this under a standing
order from a physician. Clients are more likely to access naloxone if their program provides it directly to them rather than sending them to another organization to get it. Learn more at Prescribe to Prevent (http://prescribetoprevent.org).

Helping Patients Cope With Bias and Discrimination
Patients taking medication for OUD must deal with people—including family members, friends, colleagues, employers, and community members—who are misinformed or biased about the nature of OUD and effective treatments for it.

Wherever possible, such as in a counseling session or a community education forum, counter misunderstandings with accurate information. Emphasize the message that addiction is governed by more powerful brain forces than those that determine habits. As a result, having a lot of positive intent, wanting to quit, and working hard at it sometimes won't be enough.

Remind patients about building recovery capital and sticking with their treatment plan and goals. A particularly good opportunity to do so arises when patients ask how to "get off medication." Statements such as "The longer you take medication, the more of your life you can get back and the less likely you are to return to opioid use" and "We usually recommend continuing medication long term because it helps people maintain recovery" can help clients understand that they are following medical recommendations and doing a good job of caring for themselves.

People may think that addiction is just a bad habit or willful self-destruction and that someone who has difficulty stopping opioid misuse is lazy. They may view OUD medication as "just another drug" and urge patients to stop taking it.

Review a client's motivation for tapering or quitting medication and have a conversation about the best timing for such a change. If the client has consented to communication with other providers, inform the client's prescriber about the client's desires or intent so that shared decision making can take place.

Be proactive in dispelling myths and providing facts about medications for OUD when countering misconceptions and judgmental attitudes. Point out that multiple organizations consider individuals to be in recovery if they take OUD medication as prescribed, including:

- The American Medical Association.[206]
- The American Society of Addiction Medicine.[207]
- The National Institute on Drug Abuse.[208]
- The Office of the Surgeon General.[209]
- SAMHSA.[210]
- The World Health Organization.[211]

Explain that alcohol and opioids are different substances with different effects on the body and brain. This counters the mistaken belief that people receiving buprenorphine or methadone are always "high" and as impaired as if they drank alcohol all day. People acquire tolerance to impairments that drinking causes in motor control and cognition. But this tolerance is partial; alcohol consumption always results in some deficits. Opioids don't have the same motor or cognitive effects. Complete tolerance develops to the psychoactive effects and related motor impairments opioids cause.

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[206] American Medical Association. (2017). End the epidemic. Retrieved October 23, 2017, from https://www.end-opioid-epidemic.org/types/ama

[207] 143 Kampman, K., & Jarvis, M. (2015). American Society of Addiction Medicine (ASAM) national practice guideline for the use of medications in the treatment of addiction involving opioid use. *Journal of Addiction Medicine, 9*(5), 358–367.

[208] National Institute on Drug Abuse. (n.d.). Effective treatments for opioid addiction. Retrieved October 23, 2017, from https://www.drugabuse.gov/publications /effective-treatments-opioid-addiction/effective -treatments-opioid-addiction

[209] Office of the Surgeon General. (2016). *Facing addiction in America: The Surgeon General's report on alcohol, drugs, and health.* Washington, DC: Department of Health and Human Services.

[210] Center for Substance Abuse Treatment. (2005). *Medication-assisted treatment for opioid addiction in opioid treatment programs.* Treatment Improvement Protocol (TIP) Series 43. HHS Publication No. (SMA) 12-4214. Rockville, MD: Substance Abuse and Mental Health Services Administration.

[211] Equal Employment Opportunity Commission. (1992). *A technical assistance manual on the employment provisions (Title I) of the Americans with Disabilities Act.* Washington, DC: Author.

If a person takes a therapeutic dose of opioid agonist medication as prescribed, he or she may be as capable as anyone else of driving, being emotionally open, and working productively. Some people worry that OUD medication causes a "high" because they've seen patients taking OUD medication whose behavior was affected by other substances (e.g., benzodiaze-pines). Others may assume that someone is high on a medication for OUD who isn't taking any such medication at all.

Point out that many thousands of people are prescribed medication for OUD every year, are receiving appropriate treatment, and are indistinguishable from other people. People taking OUD medication rely on it to maintain daily function, like people with diabetes rely on insulin. Nevertheless, some people think that individuals taking buprenorphine or methadone are still addicted to opioids, even if they don't use illicit drugs. For people with OUD, the medication addresses the compulsion and craving to use. It also blocks the euphoric effects of illicit opioids, which over time helps people stop attempting to use. For people with diabetes, medication addresses the problems caused by inadequate production of insulin by the pancreas. Medication allows both populations to live life more fully.

It would be inappropriate for a medical team to refuse radiation for cancer patients because the team believes chemotherapy is always needed, or to refuse chemotherapy because they believe that radiation is always needed, regardless of each patient's diagnosis and condition. It would be just as inappropriate to refuse evidence-based treatment with medication for a patient with OUD, when that may be the most clinically appropriate course of treatment.

Focus on common ground—all patients want a healthy recovery and judging or isolating someone for return to use doesn't aid anyone's recovery. A divide may occur between

patients in a group setting over return to opioid use. People in the OUD community typically are forgiving of return to opioid use and recognize that it can occur on the path to long-term recovery. However, some people in mutual-help communities judge those who return to use (see the "Helping Clients Find Accepting Mutual-Help Groups" section). Address judgmental attitudes through this analogy: People with diabetes whose blood sugar spikes aren't condemned and ejected from treatment.

Dispel the myth that OUD medications make people sick. In fact, methadone and buprenorphine relieve opioid withdrawal, even if patients don't feel complete relief in the first few days. Taking naltrexone too soon after opioid use can cause opioid withdrawal, but withdrawal symptoms can generally be managed successfully. Point out that people taking medication for OUD sometimes get colds, the fu, or other illnesses, like everyone else. A similar misconception is that OUD medications make all patients sleepy.

When return to opioid use comes up in a group counseling setting, messages about getting back on track and avoiding shaming and blaming apply just as much to the patients taking OUD medication as to other participants. This topic is an opportunity to **address the dangers of overdose, especially the dangers of using an opioid after a period of abstinence or together with other CNS depressants.**

Helping Patients Advocate for Themselves

Educate clients so they can advocate for their treatment and personal needs. Key topics include:

- Addiction as a chronic disease influenced by genetics and environment.
- The ways that medications for OUD work.
- The process of dose stabilization.
- The benefits of longer-term medication use and risks of abrupt treatment termination.
- The role of recovery supports (e.g., mutual-help groups) in helping achieve goals.

Offer clients' family and friends education on these topics as well so that they can advocate for their loved ones. Encourage patients to let family and friends know how important they are and how valuable their support is. Also urge patients to ask loved ones to help them express concerns or fears.

Role-playing can help patients self-advocate.
It allows them to practice what to say, what reactions to expect, and ways to respond. Coach patients in active listening and in focusing on solutions rather than problems.
Urge patients to advocate for themselves beyond one-on-one conversations.
Options include sharing educational pamphlets, inviting loved ones to a counseling session, or referring them to websites.

Addressing Discrimination Against Clients Who Take OUD Medication

Patients can face discriminatory actions when dealing with individuals, organizations, or systems that make decisions based on misinformation about, or biases against, the use of medication for OUD. The following sections highlight issues patients taking OUD medication may face and how counselors can help.

Help clients address employment-related issues

Under the Americans With Disabilities Act, employers cannot discriminate against patients taking medication for OUD.[212]
However, the law doesn't always stop employers from taking such action. For example, some employers conduct workplace urine drug testing, either before offering employment or randomly during employment. The OUD medication they test for most frequently is methadone, but it's possible to test for buprenorphine. Naltrexone is generally not tested for. The TIP expert panel concludes, based on multiple patient experiences, that patients who take OUD medication find it intimidating to explain to their employers why their urine test results are positive

[212] Equal Employment Opportunity Commission. (1992). *A technical assistance manual on the employment provisions (Title I) of the Americans with Disabilities Act.* Washington, DC: Author.

for opioids. Yet if they offer no explanation, they don't get the callback for the job or are let go from the job they have.

Direct patients to legal resources and help them consider how to respond to discrimination at work based on misinterpreted drug tests. Offer to speak with their prospective/ current employers to address concerns and misperceptions about OUD medication and its effect on their ability to do work tasks.

Becoming a Certified Medication-Assisted Treatment Advocate
The National Alliance for Medication Assisted Recovery has a training and credentialing program for interested people—not just those who receive medication for OUD—to become Certified Medication-Assisted Treatment Advocates (www.methadone.org/certifcation /faq.html).

Understand potential legal issues
This section describes issues that can affect access to care for patients involved in the justice system who take buprenorphine or methadone for OUD. These issues usually don't apply for naltrexone.

Many jails (short term) and prisons (long term) restrict or disallow access to OUD medication
despite the federal mandate that people who are incarcerated have access to medical care.[213] For example:

- A jail may not continue methadone treatment or allow methadone delivery by patients' OTPs.
- Patients' medication may be seized upon arrest.
- Jail health officials may deny patients' buprenorphine prescriptions.

Help negotiate patient access to OUD medication during incarceration.
Negotiating access to OUD medication can be problematic and often requires

[213] Friedmann, P. D., Hoskinson, R., Gordon, M., Schwartz, R., Kinlock, T., Knight, K., ... Frisman, L. K. (2012). Medication-assisted treatment in criminal justice agencies affliated with the Criminal Justice-Drug Abuse Treatment Studies (CJ-DATS): Availability, barriers & intentions. *Substance Abuse, 33*(1), 9–18.

multiple meetings between care providers and jail staff members to resolve successfully. Patients taking OUD medication may be forced to go without medication during incarceration. This increases their risk for opioid overdose if they return to use after reentering the community, given the decreased tolerance that results from interrupted treatment.

Encourage patients to reengage in treatment as soon as they're released. People with OUD released from prison or jail who don't take OUD medication have higher risk of overdose death during their first few weeks in the community. Early after release, they are at very high risk of overdose, given possible:

- Decrease in opioid tolerance while incarcerated.
- Lack of appropriate OUD therapy while incarcerated.
- OUD medication initiation right before release.
- Release without coordination or a slot for community-based treatment.

Patients who aren't opioid tolerant need a lower starting dose that prescribers will increase more slowly than usual. Extended-release injectable naltrexone can be an effective alternative for these patients.

Support patients in getting legal advice or counsel via their OUD medication prescribers' healthcare organization. Members of the TIP expert panel have observed situations in which law enforcement personnel arrested patients leaving methadone clinics and charged them with driving under the influence or arrested them after finding buprenorphine prescription bottles in their cars. Discussions among treatment organizations and local law enforcement leadership can help address such situations.

Address concerns and advocate for addiction specialists to select treatments best suited for each patient. Sometimes, authorities insist that patients enter a particular kind of treatment or follow particular rules related to their OUD. To ensure a patient-centered focus, help involve addiction specialists in determining what kind of treatment best meets patients' needs. This kind of advocacy works best when counselors and the programs for which they work have preexisting

relationships with personnel in local employment, law enforcement, drug court, and child welfare facilities.

Address issues in dealing with healthcare providers

Misunderstandings about OUD and its treatment aren't rare among healthcare providers:

- Patients admitted to the hospital for medical issues may face prejudice from hospital staff members.
- Providers may not know how to manage patients' OUD medication during their hospital stay.
- Some providers don't know how to manage pain in someone taking medication for OUD.

Help communicate issues to patients' prescribers, who can advocate for proper handling of OUD medication. It is also possible to help hospital staff members see the patient as a whole person who deserves respect and to provide them with essential information about treatment for OUD.

Inpatient SUD treatment facilities may refuse admission until patients are off buprenorphine or methadone. Sometimes, patients taking OUD medication seek admission to inpatient facilities for treatment of an additional SUD, a mental disorder, or both. If a facility won't accept someone on OUD medication, call on local or state regulatory authorities (e.g., the State Opioid Treatment Authority) and patients' healthcare professionals to intervene with the facility's professional staff and management.

Demonstrate awareness of pregnancy and parenting issues

Healthcare professionals may be unaware of current guidelines for treating pregnant women with OUD. As a result, they may inappropriately:

- Deny OUD medication to pregnant women.
- Discourage breastfeeding by mothers taking OUD medication.

- Direct women who become pregnant while taking OUD medication to undergo withdrawal from their medication and attempt abstinence.

Hospital policies on screening infants for prenatal substance exposure vary considerably.
A positive screen may trigger involvement of Child Protective Services. This may occur even when the positive screen results from treatment with OUD medication under a physician's care rather than opioid misuse.

Help pregnant and postnatal clients in these situations by:
- **Educating them** and encouraging them to share pertinent information and resources with healthcare professionals involved in their care.
- **Coordinating with their prescribers** to help them get prenatal and postnatal care from well-informed healthcare professionals.
- **Getting involved in efforts to educate the local healthcare community** about best practices for the care of pregnant and postnatal women with OUD.

Legal problems can arise if Child Protective Services or legal personnel don't understand that parents receiving OUD medication are fully capable of caring for children and contributing to their families. Judges, probation or parole officers, or Child Protective Services workers may inappropriately request that patients discontinue medication as a condition of family reunification. Such orders are medically inappropriate and should be challenged. Possible ways to help:

- **Write letters to judges and lawyers** explaining how effective OUD medication can be.
- **Send judges and lawyers literature** about current medical recommendations (including this TIP).
- **Testify in court,** if necessary.

Helping Clients Find Accepting Mutual- Help Groups

Voluntary participation in 12-Step groups can improve abstinence and recovery-related skills and behaviors for some people with SUDs. Greater involvement (e.g., being a 12-Step sponsor) can increase these benefits.[214] However, not much research has explored less widespread types of groups (e.g., groups that follow a given religion's principles, secular groups that downplay the spiritual aspects of 12-Step groups). Research exploring longitudinal outcomes for people with OUD who attend NA is limited, but findings link more frequent attendance with abstinence.[215]

Clients taking medication for OUD may face challenges in attending mutual-help groups.

For example:

- NA, the most widely available program, treats illicit opioids and OUD medications equally in gauging abstinence and recovery. NA doesn't consider people taking OUD medication "clean and sober."[216]
- Local chapters of NA may decide not to allow people taking OUD medication to participate at meetings or may limit their participation (e.g., not allowing service work).
- Clients attending some NA meetings may encounter hostile attitudes toward the use of medication.
- AA's official policy is more accepting of the use of prescribed medication, but clients may still encounter negative attitudes toward their use of medications for OUD.
- Other groups, such as some religious mutual-help programs, SMART Recovery, and LifeRing Secular Recovery, also have policies that could challenge clients for taking medication for OUD.

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[214] Donovan, D. M., Ingalsbe, M. H., Benbow, J., & Daley, D. C. (2013). 12-step interventions and mutual support programs for substance use disorders: An overview. *Social Work in Public Health, 28*(3–4), 313–332.

[215] Monico, L. B., Gryczynski, J., Mitchell, S. G., Schwartz, R. P., O'Grady, K. E., & Jaffe, J. H. (2015). Buprenorphine treatment and 12-step meeting attendance: Conficts, compatibilities, and patient outcomes. *Journal of Substance Abuse Treatment, 57,* 89–95.

[216] Narcotics Anonymous World Services. (2016). *Narcotics Anonymous and persons receiving medication-assisted treatment.* Chatsworth, CA: Author.

Clients will be better able to find supportive mutual-help groups if their counselor and program:

Evaluate attitudes toward medication for OUD among local mutual-help groups.

- **Keep on hand information** about all mutual-help options available in the clients' area.
- **Recruit volunteers from mutual-help groups** to help clients find and attend meetings (e.g., by providing transportation, serving as "sponsors," introducing clients).
- **Do not mandate meeting attendance.** Recommending participation is just as effective.[217]
- **Keep track of clients' experiences at different groups** to ensure that meetings remain welcoming.
- **Help clients start onsite mutual-help groups.**
- **Ask staff members to evaluate their own feelings and beliefs** about mutual-help groups.

Facilitate positive mutual-help group experiences

- **Educate clients about mutual-help groups.** Explore group types, risks and benefits of participation, and limitations of research in support of those risks and benefits.
- **Suggest buddying up.** Clients can attend meetings with other people who take medication for OUD.
- **Review with clients their understanding of and prior experience with mutual help.**
- **Explore clients' understanding of the benefits and risks of disclosure** about taking OUD medication.
- **Develop a risk-reduction plan** for disclosure if clients want to share their use of OUD medication (e.g., talking with an individual group member instead of disclosing to the entire group).

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[217] Monico, L. B., Gryczynski, J., Mitchell, S. G., Schwartz, R. P., O'Grady, K. E., & Jaffe, J. H. (2015). Buprenorphine treatment and 12-step meeting attendance: Conficts, compatibilities, and patient outcomes. *Journal of Substance Abuse Treatment, 57,* 89–95.

Help clients anticipate and learn to handle negative responses: Develop sample scripts clients can use when questioned about their medication.
Role-play scenarios in which clients respond to questions about their use of medication.

Respect the privacy of clients' participation in mutual-help groups and recognize that some groups ask that participants not discuss what occurs in meetings.
Make sure clients know they can talk about their experiences in mutual-help groups but don't pressure them to disclose in these groups that they take OUD medication.
Consider mutual-help participation using groups more open to OUD medication (e.g., attending AA even if the client has no alcohol use disorder; attending groups for co-occurring substance use and mental disorders, such as Dual Recovery Anonymous or Double Trouble in Recovery). Clients with OUD who attend AA and not NA have similar recovery-related outcomes and retention rates.[218]

Online mutual-help groups

Before recommending an online group, check its content and tone on the use of medication.

Mutual help using the Internet (either through real-time chat rooms or discussion boards where one posts and waits for responses) has been growing in popularity. This is an especially valuable resource for clients living in rural and remote areas. Groups range from general meetings for people with a particular SUD (e.g., online AA meetings) to those that are very specific (e.g., Moms on Methadone). Moderated groups are preferable to unmoderated groups. TIP 60, *Using Technology-Based Therapeutic Tools in Behavioral Health Services*, addresses many of the pros and cons of online support groups.

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[218] 164 Kelly, J. F., Greene, M. C., & Bergman, B. G. (2014). Do drug-dependent patients attending Alcoholics Anonymous rather than Narcotics Anonymous do as well? A prospective, lagged, matching analysis. *Alcohol and Alcoholism, 49*(6), 645–653.

Mutual-help groups specific to OTPs

Although these meetings occur mostly on the premises of OTPs, it may be possible to use the models developed by OTPs in more general SUD treatment settings. Because they serve only patients receiving medication to treat OUD, OTPs can create and sustain onsite mutual-help groups specific to this population. Such groups include Methadone Anonymous (MA),[219] other variations on a 12-Step model,[220] 170 and the mutual-help component of Medication- Assisted Recovery Services (MARS). MARS is a recovery community organization, not just a mutual-help program. MARS members design, implement, and evaluate a variety of peer-delivered recovery support services in addition to providing meetings.

Facilitating Groups That Include Patients Taking OUD Medication

Foster acceptance via attitude and behavior when facilitating groups that include patients taking OUD medication:

- **Establish ground rules** about being respectful, avoiding negative comments about group members, and keeping statements made in the group confidential—as with any group.
- **Be proactive.** State up front that ground rules apply to everyone, regardless of a given person's decisions about whether to include OUD medication in his or her path to recovery.
- **Ask members to discuss how to address any negative comments,** should they occur. This is especially important for mixed groups.
- **Ask group members to affirm that they will abide by the rules.**
- **Provide consistent reminders** throughout each session about the ground rules.

Group members may still make negative comments about medication for OUD. Avoid feeding the negativity with attention, which can worsen the situation.

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[219] Ginter, W. (2012). Methadone Anonymous and mutual support for medication-assisted recovery. *Journal of Groups in Addiction and Recovery, 7*(2–4), 189–201.

[220] Ronel, N., Gueta, K., Abramsohn, Y., Caspi, N., & Adelson, M. (2011). Can a 12-step program work in methadone maintenance treatment? *International Journal of Offender Therapy and Comparative Criminology, 55*(7), 1135–1153.

Reframe negative comments to express underlying motivations, often based on fear or misunderstanding.

Remain positive; model expected behavior, which can benefit the person who made the negative remark.

Additional tips for leading mixed groups include the following:

- **Treat patients taking OUD medication the same as other patients in the group.** Patients taking medication can participate in and benefit from individual and group counseling just like other patients. There is no need to have separate counseling tracks
- based on OUD medication status, nor should that status limit a participant's responsibilities, leadership role, or level of participation.
- **Meet with patients taking OUD medication in advance to prepare them for mixed-group settings.** Advise them that they don't have to disclose their medication status to the group, just as they don't have to disclose any other health issues. Counsel them that if they choose to talk about their medication status, it helps to talk about how medication has helped shape their personal recovery.
- **Don't single out patients taking OUD medication.** Let participants decide whether to tell the group about any issue they want to share, including medication status. If a patient chooses to disclose that status, follow up after the session to ensure that he or she is in a positive space and feels supported.
- **Keep the session's focus on the topic and not on the pros and cons of medication for OUD.** If the person receiving medication for OUD or other group members have specific questions about such medications, have them ask their healthcare professionals.
- **Reinforce messages of acceptance.** During the wrap-up discussion at the end of a session, members may comment on points that stood out for them. This is a chance to restate information accurately and model respect for each patient's road to recovery, whether it includes OUD medication or not.
- **Review confidentiality rules.** Affirm that patients' OUD medication status will not be shared with other group members. Remind participants to think carefully before sharing personal details such as their medication status with the

group, because other participants may not respect confidentiality even if they have agreed to do so as part of the group guidelines.

3. Other Common Counseling Concerns

Patients must sign releases to permit ongoing conversations between care providers in accordance with federal regulations on confidentiality of medical records for patients in treatment for an SUD (42 CFR Part 2). When patients' primary care providers, prescribers of medication for OUD, and addiction-specific counselors don't work for the same entity, patients must consent for them to share information.

It can be challenging when a patient refuses to consent to collaborative communication among his or her healthcare team members.
In these cases, the professionals involved must decide whether they will continue to provide either medication or counseling services without permission to collaborate. In other words, is cross-communication among all providers required for collaborative care? The answer to this complicated question depends on each patient's circumstances.

The TIP expert panel recommends communication among providers as the standard of care for OUD treatment and recovery support.

Carefully consider deviations from this standard, which should occur only rarely. That said, individualize decisions about collaborative communication among providers to each patient's unique preferences, needs, and circumstances.

Patients may not consent to communication among providers if they:

- **Have experienced discrimination in healthcare systems.**
- **Have developed OUD after taking opioid pain medication.**

- **Have legitimate cause not to trust providers** (e.g., perceiving themselves as having been abused by a healthcare professional).[221]

Are not ready to make primary care providers aware of their disorder, even
- (or especially) if those providers have been prescribing opioid pain medication.
- **Encounter problems in making progress toward recovery.** After typically consenting to communication among providers, a patient's sudden revocation may signal trouble in recovery.
- Exhibit 4.16 lists common collaborative care issues and responses counselors can consider. Suggested responses assume that patients have consented to open exchange of information among all providers.

Exhibit 4.16. Common Collaborative Care Issues and Possible Counselor Responses

POTENTIAL MEDICATION-RELATED ISSUE	**COUNSELOR RESPONSE**
The patient complains of continued cravings.	Talk with the patient about his or her medication adherence. Review with the patient strategies for overcoming cravings using a CBT model. Communicate with the prescriber to see whether dosage can be adjusted to subdue the cravings.
A patient taking methadone does not appear engaged in counseling sessions and	Ask the patient whether drowsiness is caused by lack of sleep, disturbed sleep, substance use, or overmedication. Consider obtaining a spot urine test (if available). In all cases of drowsiness, alert the prescriber

[221] Palis, H., Marchand, K., Peng, D., Fikowski, J., Harrison, S., Spittal, P., … Oviedo-Joekes, E. (2016). Factors associated with perceived abuse in the health care system among long-term opioid users: A cross-sectional study. *Substance Use and Misuse, 51*(6), 763–776.

seems drowsy during conversations.	immediately so that the cause can be determined. This is particularly important during the first few weeks of treatment.
The patient is at risk for return to opioid use.	Inform the prescriber if the patient appears at risk for return to use given cravings, life stressors, changes in social circumstances, new triggers, or the like. This alerts the prescriber to monitor the patient more closely and consider medication changes to reduce likelihood of return to use.
The patient has recently returned to opioid misuse after a period of abstinence.	Gather details about circumstances surrounding the incident of use and, in collaboration with the prescriber and the patient, adjust the treatment plan accordingly. Reinforce the patient's understanding of the increased risk of opioid overdose given altered levels of tolerance.
The patient is discussing chronic pain with the counselor.	Direct the patient to a healthcare professional for assessment of pain and medical treatment as necessary. If indicated as appropriate by a healthcare professional, provide CBT for dealing with pain or instruct the patient in adjunct methods for pain relief (e.g., meditation, exercise, physical therapy).
The patient is asking the counselor for medical advice on what dose to take, side effects, how long to stay on the medication, and the like.	Answer questions based on your knowledge of medications for treatment of OUD but don't provide medical advice. Refer the patient to the prescriber for that. As appropriate, contact the prescriber with the patient to have a three-way discussion.
The counselor or patient is concerned that the prescriber is not giving quality care.	As appropriate, advocate for the patient with the prescribing medical team.

The patient discloses use of other drugs.	Use motivational interviewing techniques to have a collaborative conversation about the details of this drug use. For example, give a response like "Tell me more about this," followed by questions about the specific drugs used, why they were used, and what the patient's thoughts are about changing that drug use.
The patient discloses that she is pregnant.	Advise the patient to contact her prescriber immediately no matter what medication she is taking. Work with her to help her get access to prenatal care (if she doesn't have it already) and other health services related to pregnancy as needed.
The patient has a positive urine screen.	Using motivational interviewing tools, discuss with the patient the context of the substance use and what implications this use may have for the treatment plan. If the patient denies the substance use, reconsider the patient's readiness to change and how it affects the treatment plan.

Resources Related to Medications for Opioid Use Disorder

General Resources

Facts and Figures

American Association for the Treatment of Opioid Dependence (AATOD), Frequently Asked Questions (www.aatod.org/resources /frequently-asked-questions).

Centers for Disease Control and Prevention (CDC), Smoking & Tobacco Use (www.cdc.gov /tobacco/index.htm).

Legal Action Center (LAC), Medication- Assisted Treatment for Opioid Addiction: Myths and Facts (http://lac.org/wp-content /uploads/2016/02/Myth-Fact-for-MAT.pdf).

Missouri Department of Mental Health, Methadone Maintenance Myths and Resources
(https://dmh.mo.gov/docs/ada/methadonemyths .pdf).
National Institute on Drug Abuse (NIDA)
(www.drugabuse.gov):
Addiction Science (www.drugabuse.gov /related-topics/addiction-science). Provides two short videos that explain the nature of addiction. These are useful in educating people in primary care who suffer from addiction. This site has links to publications for professionals that explain the nature of addiction.

NIDAMED, Medical and Health Professionals (www.drugabuse.gov/nidamed-medical -health-professionals). Disseminates science-based resources to healthcare professionals on the causes and consequences of drug use and addiction and advances in pain management.

Office of National Drug Control Policy, Medication-Assisted Treatment for Opioid Addiction (https://online.ndbh.com/docs /providers/SubstanceUseCenter/Medication -Assisted-Treatment-Edited.pdf): Offers a factsheet with a useful summary of pharmacotherapy for OUD and its effectiveness.
Partnership for Drug-Free Kids, Commentary: Countering the Myths About Methadone
(www.drugfree.org/news-service/commentary -countering-the-myths-about-methadone).

Substance Abuse and Mental Health Services Administration (SAMHSA):
Addiction Technology Transfer Center **(ATTC)** (http://attcnetwork.org/home). Network with 10 regional centers across the country that provide training and information on evidence-based practices to practitioners. The ATTC website's section on OUD medication has many resources for clinicians, patients, and family members (www.attcnetwork.org /explore/priorityareas/wfd/mat/mat.pubs.asp).

- State Opioid Treatment Authorities (SOTAs) (https://dpt2.samhsa.gov/regulations/smalist .aspx).

United States Surgeon General's Report,
Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health (https://addiction.surgeongeneral.gov).

Groups and Organizations
AATOD (www.aatod.org): Works with federal and state agencies on opioid treatment policy throughout the United States. Convenes conferences every 18 months on evidence-based clinical practice, current research, and organizational developments related to OUD treatment. AATOD develops publications that serve as resources for addiction counselors and peer support providers.

American Academy of Addiction Psychiatry (AAAP) (www.aaap.org): Offers education and training materials on addiction psychiatry (e.g., webinars, continuing medical education courses).

American Society of Addiction Medicine (ASAM) (www.asam.org): Provides medical education and resources on the treatment of SUDs, including OUD.
LAC (https://lac.org): Offers information about the rights of people with criminal records, HIV/AIDS, and SUDs.

Medical Assisted Treatment of America (www.medicalassistedtreatment.org): Raises awareness and understanding of substance misuse, the problems it creates, and ways to address these problems.

National Alliance for Medication Assisted Recovery (NAMA Recovery) (www.methadone .org): Supports quality opioid agonist treatment through its many U.S. chapters and its international network of affiliate chapters. Thousands of methadone clients and healthcare professionals belong to the organization.

National Alliance of Advocates for Buprenorphine Treatment (www.naabt.org): Aims to educate the public about opioid addiction and buprenorphine as a

treatment option, to reduce prejudice and discrimination against clients who have SUDs, and to connect clients in need to qualified treatment providers.

SAMHSA (www.samhsa.gov):

- Buprenorphine Practitioner Verification for Pharmacists (www.samhsa.gov/bupe /lookup-form)
- National Recovery Month (https://recovery month.gov)
- Opioid Treatment Program (OTP) Directory (https://dpt2.samhsa.gov/treatment)
- SOTAs (https://dpt2.samhsa.gov/regulations /smalist.aspx)

SAMHSA Publications

All publications listed in this section are available for free from SAMHSA's publications ordering webpage (https://store.samhsa.gov) or by calling 1-877-SAMHSA-7 (1-877-726-4727):

- TIP 42: *Substance Abuse Treatment for Persons With Co-Occurring Disorders* (https://store.samhsa.gov/product /TIP-42-Substance-Abuse-Treatment-for -Persons-With-Co-Occurring-Disorders /SMA13-3992)
- TIP 54: *Managing Chronic Pain in Adults With or in Recovery From Substance Use Disorders* (https://store.samhsa.gov/product/TIP-54 -Managing-Chronic-Pain-in-Adults-With-or -in-Recovery-From-Substance-Use-Disorders /SMA13-4671)
- TIP 57: *Trauma-Informed Care in Behavioral Health Services* (https://store.samhsa.gov /product/TIP-57-Trauma-Informed-Care-in -Behavioral-Health-Services/SMA14-4816)
- TIP 62: *Relapse Prevention and Recovery Promotion in Behavioral Health Services* (Once published, this TIP will be available on SAMHSA's publications ordering webpage, https://store.samhsa.gov)
- *Advisory:* An Introduction to Extended- Release Injectable Naltrexone for the Treatment of People With Opioid Dependence (https://store.samhsa.gov /product/An-Introduction-to-Extended -Release-Injectable-Naltrexone-for-the -Treatment-of-People-with-Opioid -Dependence/SMA12-4682)

- *Advisory:* Sublingual and Transmucosal Buprenorphine for Opioid Use Disorder: Review and Update (https://store.samhsa .gov/product/Advisory-Sublingual-and -Transmucosal-Buprenorphine-for-Opioid -Use-Disorder-Review-and-Update /SMA16-4938)
- *Clinical Guidance for Treating Pregnant and Parenting Women With Opioid Use Disorder and Their Infants* (https://store.samhsa.gov /product/Clinical-Guidance-for-Treating -Pregnant-and-Parenting-Women-With -Opioid-Use-Disorder-and-Their-Infants /All-New-Products/SMA18-5054)
- *Clinical Use of Extended-Release Injectable Naltrexone in the Treatment of Opioid Use Disorders: A Brief Guide* (https://store .samhsa.gov/shin/content//SMA14-4892 /SMA14-4892.pdf)
- *A Collaborative Approach to the Treatment of Pregnant Women With Opioid Use Disorders* (https://store.samhsa.gov/product/A -Collaborative-Approach-to-the-Treatment -of-Pregnant-Women-with-Opioid-Use -Disorders/SMA16-4978)
- *Decisions in Recovery: Treatment for Opioid Use Disorders, Handbook* (https://store .samhsa.gov/product/SMA16-4993)
- Integrated Treatment for Co-Occurring Disorders Evidence-Based Practices (EBP) Kit (https://store.samhsa.gov/product/Integrated -Treatment-for-Co-Occurring-Disorders -Evidence-Based-Practices-EBP-KIT /SMA08-4367)
- Technical Assistance Publication 32: *Clinical Drug Testing in Primary Care* (https://store .samhsa.gov/shin/content//SMA12-4668 /SMA12-4668.pdf)
- *What Are Peer Recovery Support Services?* (https://store.samhsa.gov/shin/content /SMA09-4454/SMA09-4454.pdf)

General Information

Agency for Healthcare Research and Quality:

- *Medication-Assisted Treatment Models of Care for Opioid Use Disorder in Primary Care Settings* (www.ncbi.nlm.nih.gov/books /NBK402352)
- Academy for Integrating Behavioral Health and Primary Care (https://integrationacademy .ahrq.gov)

American Academy of Family Physicians:

- Chronic Pain Management and Opioid Misuse: A Public Health Concern (Position Paper) (www.aafp.org/about/policies/all/pain -management-opioid.html)
- Pain Management and Opioid Use Resources (www.aafp.org/patient-care/public-health /pain-opioids/resources.html)

ATTC Network (http://attcnetwork.org/home): This nationwide network of SAMHSA-sponsored regional centers is a multidisciplinary resource for professionals in the addiction treatment and recovery services fields. The network has many valuable resources and projects of interest to people involved in treating SUDs. Of particular interest to readers of this TIP are the training programs produced as part of the NIDA/ SAMHSA-ATTC Blending Initiative:

- Buprenorphine Treatment: Training for Multidisciplinary Addiction Professionals (www.attcnetwork.org/projects/buptx.aspx)
- Buprenorphine Treatment for Young Adults (www.attcnetwork.org/projects/bupyoung.aspx)
- Prescription Opioid Addiction Treatment Study (POATS) (www.attcnetwork.org/projects /poats.aspx)

BupPractice.com Federal Recordkeeping Requirements for Buprenorphine Treatment
(www.buppractice.com/node/12246): Provides information about federal recordkeeping requirements.

CDC Smoking & Tobacco Use (www.cdc.gov /tobacco/index.htm): Includes resource links for clinicians on smoking and the treatment of tobacco use.

Centers for Medicare & Medicaid Services
(www.cms.gov/Medicare/Medicare-General -Information/Telehealth/index.html): Gives guidance on the delivery of telehealth.

Department of Health and Human Services (HHS):

- Centers for Medicare & Medicaid Services Clinical Laboratory Improvement Amendments Application for Certification (www.cms.gov/Medicare/CMS-Forms/CMS -Forms/downloads/cms116.pdf)

- Medication Assisted Treatment for Opioid Use Disorders: Final Rule (www.federalregister .gov/documents/2016/07/08/2016-16120 /medication-assisted-treatment-for-opioid -use-disorders)

Drug Enforcement Administration (DEA):

- DEA Requirements for DATA Waived Physicians (www.deadiversion.usdoj.gov/pubs /docs/dwp_buprenorphine.htm). Lists DEA requirements for Drug Addiction Treatment Act of 2000 (DATA 2000)-waivered healthcare professionals.
- Form DEA-106, Report of Theft or Loss of Controlled Substances (https://apps .deadiversion.usdoj.gov/webforms/dtlLogin .jsp). Provides instructions for completing form DEA-106, which must be fled when stored buprenorphine is lost or stolen.
- *Practitioner's Manual* (www.deadiversion .usdoj.gov/pubs/manuals/pract). Provides guidance on how to comply with federal requirements on recordkeeping for ordering, storing, and dispensing buprenorphine in the office. This manual is from the DEA's Office of Diversion Control.

Drugs.com:

- Buprenorphine Drug Interactions (www.drugs .com/drug-interactions/buprenorphine-index .html?flter=3&generic_only=)
- Drug Interactions Checker (www.drugs.com /drug_interactions.php)

FDA:

- Approved Risk Evaluation and Mitigation Strategy (REMS): Buprenorphine Transmucosal Products for Opioid Dependence (www .accessdata.fda.gov/scripts/cder/rems/index .cfm?event=RemsDetails.page&REMS=9)
- REMS: Probuphine (buprenorphine hydrochloride) (www.accessdata.fda.gov/scripts /cder/rems/index.cfm?event=IndvRemsDetails .page&REMS=356)

- REMS: Sublocade (extended-release injectable buprenorphine) (www.accessdata.fda.gov /scripts/cder/rems/index.cfm?event =IndvRemsDetails.page&REMS=376)
- REMS: Suboxone/Subutex (buprenorphine and naloxone/buprenorphine) (www.accessdata .fda.gov/scripts/cder/rems/index.cfm?event =IndvRemsDetails.page&REMS=352)
- REMS: Vivitrol (extended-release naltrexone [XR-NTX]) (www.vivitrolrems.com)

LAC (https://lac.org): LAC attorneys provide legal advice by phone to service providers and government agencies. They assist dozens of agencies annually with questions about confidentiality of treatment records, discrimination, and other issues. LAC's confidentiality hotline provides information about the federal law protecting the confidentiality of drug and alcohol treatment and prevention records (42 CFR Part 2). The hotline is free to New York treatment providers and government agencies. Outside New York, the hotline is accessible if the state alcohol/drug oversight agency subscribes to LAC's Actionline service. To speak with a hotline attorney, call LAC Monday through Friday 1–5 p.m. (Eastern Time Zone) at 1-212-243-1313, or toll-free at 1-800-223-4044.

National Alliance of Advocates for Buprenorphine Treatment 30–100 Patient Limit (www.naabt.org/30_patient_limit.cfm): Summarizes the DATA 2000 law.

National Association of State Controlled Substances Authorities State Profiles (www .nascsa.org/stateprofles.htm): Contains a directory of each state's prescription drug monitoring program (PDMP).

National Conference of State Legislatures Drug Overdose Immunity and Good Samaritan Laws (www.ncsl.org/research/civil-and-criminal -justice/drug-overdose-immunity-good-samaritan -laws.aspx): Provides information about naloxone and Good Samaritan immunity.

National Institute on Alcohol Abuse and Alcoholism (**NIAAA) Professional Education Materials** (www.niaaa.nih.gov/publications /clinical-guides-and-manuals): Provides professional education materials; offers links to screening, treatment planning, and general information for clinicians in outpatient programs.

National Library of Medicine's DailyMed:

- FDA label information for methadone (https:// dailymed.nlm.nih.gov/dailymed/search .cfm?labeltype=all&query=METHADONE)
- FDA label information for naltrexone (https:// dailymed.nlm.nih.gov/dailymed/drugInfo.cfm ?setid=cd11c435-b0f0-4bb9-ae78 - 60f101f3703f)

NIDA:

- Available Treatments for Marijuana Use Disorders (www.drugabuse.gov/publications /research-reports/marijuana/available - treatments-marijuana-use-disorders). Provides information about treatment options for individuals with marijuana use disorder.
- Opioid Overdose Reversal With Naloxone (Narcan, Evzio) (www.drugabuse.gov/related -topics/opioid-overdose-reversal-naloxone -narcan-evzio). Contains naloxone information for providers.

- NIDAMED, Medical and Health Professionals (www.drugabuse.gov/nidamed-medical -health-professionals). Provides practice-related and professional education-related resources.
- Medications To Treat Opioid Addiction (www .drugabuse.gov/publications/research-reports /medications-to-treat-opioid-addiction /overview). Provides an overview of the need for and effcacy of OUD medications and discusses common misconceptions, impacts on outcome, and use of OUD medications with certain specific populations.
- *Effective Treatments for Opioid Addiction* (https://www.drugabuse.gov/publications /effective-treatments-opioid-addiction /effective-treatments-opioid-addiction).
- Therapeutic Communities (www.drugabuse .gov/publications/research-reports /therapeutic-communities/what-are -therapeutic-communities). Gives a brief overview of OUD medications and links to additional information.
- *Principles of Drug Addiction Treatment: A Research-Based Guide* (www.drugabuse.gov /publications/principles-drug-addiction -treatment-research-based-guide-third -edition/preface). Discusses how OUD affects the

brain and covers the state of addiction treatment in the United States, principles of effective treatment, frequently asked questions about OUD medication, evidence-based approaches to treatment, and additional resources.

- *Principles of Adolescent Substance Use Disorder Treatment: A Research-Based Guide* (www.drugabuse.gov/publications/principles -adolescent-substance-use-disorder-treatment -research-based-guide/introduction). Discusses principles of SUDs in adolescents, addresses frequently asked questions, summarizes treatment settings and evidence-based treatment approaches, and provides treatment referral resources.
- *Treating Opioid Use Disorder During Pregnancy* (www.drugabuse.gov/publications /treating-opioid-use-disorder-during -pregnancy/treating-opioid-use-disorder -during-pregnancy). Addresses the risks of OUD to the pregnant woman and the fetus, briefly summarizes OUD pharmacotherapies for use during pregnancy, and provides links to additional information.

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

Prescription Drug Abuse Policy System's Naloxone Overdose Prevention Laws (http://pdaps.org/datasets/laws-regulating -administration-of-naloxone-1501695139): Provides a map with a link to each state's naloxone overdose prevention laws, including policies on prescribing, dispensing, and civil and criminal immunity.

Project Lazarus's Naloxone: The Overdose Antidote (www.projectlazarus.org/naloxone): Provides guidance on administering naloxone.

Providers' Clinical Support System's (PCSS's) How To Prepare for a Visit From the Drug Enforcement Agency Regarding Buprenorphine Prescribing (http://pcssmat .org/wp-content/uploads/2014/02/FINAL-How -to-Prepare-for-a-DEA-Inspection.pdf): Provides a description of the DEA inspection process and how to comply with its requirements.

SAMHSA:

Dear Colleague Letters for Medication- Assisted Treatment Providers (www.samhsa .gov/medication-assisted-treatment /legislation-regulations-guidelines/dear -colleague-letters). Offers regular communications to the opioid treatment community regarding clinical and regulatory issues related to opioid treatment. Regulations, policies, and best practices for OTPs and office-based

- opioid treatment (OBOT) clinics can change, and Dear Colleague Letters help providers stay up to date.
- Understanding the Final Rule for a Patient Limit of 275 (www.samhsa.gov/sites/default /fles/programs_campaigns/medication_assisted/understanding-patient-limit275.pdf). Provides information about the final rule and how to use it to increase patient access to medication for OUD and associated reporting requirements.
- Buprenorphine Waiver Management (www .samhsa.gov/medication-assisted-treatment /buprenorphine-waiver-management). Provides information on the buprenorphine waiver, including links to the buprenorphine waiver application and an explanation of the processes, requirements, and recordkeeping strategies associated with prescribing buprenorphine.
- Qualify for Nurse Practitioners (NPs) and Physician Assistants (PAs) Waiver (www .samhsa.gov/medication-assisted-treatment /qualify-nps-pas-waivers). Provides information for NPs and PAs about the buprenorphine waiver training, with links to trainings and the application process.
- Buprenorphine Training for Physicians (www .samhsa.gov/medication-assisted-treatment /training-resources/buprenorphine-physician -training). Offers links to organizations that provide buprenorphine training for physicians.
- *SAMHSA Opioid Overdose Prevention Toolkit* (https://store.samhsa.gov/product/SAMHSA -Opioid-Overdose-Prevention-Toolkit/SMA16 -4742). Prepares healthcare professionals, communities, and local governments with material to develop practices and policies to help prevent opioid-related overdoses and deaths. It addresses issues for healthcare professionals, first responders, treatment providers, and those recovering from opioid overdose.
- *Federal Guidelines for Opioid Treatment Programs* (https://store.samhsa.gov/product /Federal-Guidelines-for-Opioid-Treatment -

Programs/PEP15-FEDGUIDEOTP). Provides updated guidelines for how OTPs can satisfy the federal regulations.

- Form SMA-168 Opioid Treatment Exception Request (www.samhsa.gov/medication -assisted-treatment/opioid-treatment -programs/submit-exception-request). Provides instructions for physicians on how to request exceptions to federal standards for opioid treatment.
- Laws and Regulations (www.samhsa.gov /about-us/who-we-are/laws-regulations). Provides an overview and summary of the most frequent questions about disclosure and patient records pertaining to substance use treatment that federal programs maintain.
- *Substance Abuse in Brief Fact Sheet:* Introduction to Mutual-Support Groups for Alcohol and Drug Abuse (https://store .samhsa.gov/shin/content/SMA08-4336 /SMA08-4336.pdf). Provides information to help medical and behavioral health service providers understand mutual-help groups and how to make referrals to such groups.

SAMHSA has developed several resources to guide healthcare professionals in their use of telehealth and telemedicine approaches for OUD: *In Brief:* Rural Behavioral Health: Telehealth Challenges and Opportunities (https:// store.samhsa.gov/shin/content/SMA16 -4989/SMA16-4989.pdf)
Certified Community Behavioral Health Clinics (CCBHCs) Using Telehealth or Telemedicine (www.samhsa.gov/section -223/care-coordination/telehealth -telemedicine)

Practice Guidelines and Decision- Support Tools

ASAM:

- *Appropriate Use of Drug Testing in Clinical Addiction Medicine* (http://download.lww.com /wolterskluwer_vitalstream_com/PermaLink /JAM/A/JAM_11_3_2017_06_02_SAFARIAN_JAM-D-17-00020_SDC1.pdf). Details the ASAM consensus statement on drug testing in addiction treatment.
- The ASAM Criteria (www.asam.org/quality -practice/guidelines-and-consensus -documents/the-asam-criteria). Provides criteria and a comprehensive set of guidelines for placement, continued stay, and transfer/ discharge of patients with addiction and co-occurring conditions.

- *The ASAM National Practice Guidelines: For the Use of Medication in the Treatment of Addiction Involving Opioid Use* (www.asam .org/docs/default-source/practice-support /guidelines-and-consensus-docs/asam -national-practice-guideline-supplement .pdf). Provides information on prescribing methadone, buprenorphine, naltrexone, and naloxone. The document also discusses the needs of special populations, including women during pregnancy, patients with chronic pain, adolescents, individuals in the criminal justice system, and patients with co-occurring psychiatric conditions.

CDC:

- CDC Guideline for Prescribing Opioids for Chronic Pain (www.cdc.gov/drugoverdose /prescribing/guideline.html).
- Guideline Resources: Clinical Tools (www.cdc .gov/drugoverdose/prescribing/clinical-tools .html). Provides links and tools to help clinicians prevent opioid overdose deaths.

Credible Meds (www.crediblemeds.org): Maintains a list of medications that may increase QTc intervals. Free registration is required to access the most up-to-date list.

HHS:

- BeTobaccoFree.gov News and Resources (https://betobaccofree.hhs.gov/quit-now /index.html#professionals). Offers links for clinicians that provide guidance on the care for patients with nicotine addiction. The Resources section is at the bottom of the page linked here.
- BeTobaccoFree.gov Nicotine Addiction and Your Health (https://betobaccofree.hhs.gov /health-effects/nicotine-health). Provides information on nicotine addiction and its health effects.

Institute for Research, Evaluation, and Training in Addictions' Management of Benzodiazepines in Medication-Assisted Treatment (http://ireta.org/wp-content/uploads /2014/12/BP_Guidelines_for_Benzodiazepines .pdf): Provides information on managing benzodiazepine use in patients taking medications for OUD.

PCSS for Medication Assisted Treatment (https://pcssmat.org): Provides buprenorphine waiver training for clinicians (physicians, NPs, and PAs).

PCSS Mentoring Program (https://pcssmat.org /mentoring): Gives providers guidance on prescribing OUD medications. This national network of experienced providers is available at no cost. Mentors provide support by telephone, email, or in person if possible.

PCSS Models of Buprenorphine Induction (http://pcssmat.org/wp-content/uploads/2015 /02/Buprenorphine-Induction-Online-Module .pdf): Provides information about various buprenorphine induction approaches including in-office, non-OTP, and at-home dosing.

Prescribe To Prevent (http://prescribetoprevent .org): Provides information about naloxone prescribing for overdose prevention, including educational patient handouts and videos.

SAMHSA:

- MATx Mobile App To Support Medication- Assisted Treatment of Opioid Use Disorder (https://store.samhsa.gov/apps/mat). Provides information on FDA-approved treatment approaches and medications used to treat OUD. It includes a buprenorphine prescribing guide with information on the DATA 2000 waiver process and patient limits. Clinical support tools (e.g., treatment guidelines; *International Classification of Diseases,* 10th Edition, coding; guidance on working with special populations), help lines, and SAMHSA's treatment locators are also included.
- *Pocket Guide: Medication-Assisted Treatment of Opioid Use Disorder* (https://store.samhsa .gov/shin/content/SMA16-4892PG/SMA16 -4892PG.pdf).
- Buprenorphine (www.samhsa.gov/medication -assisted-treatment/treatment/buprenorphine).
- Naltrexone (www.samhsa.gov/medication -assisted-treatment/treatment/naltrexone).
- Decisions in Recovery: Treatment for Opioid Use Disorder (https://media.samhsa.gov/MAT -Decisions-in-Recovery). Provides information on shared decision making in pharmaco-therapy for OUD.

- Decisions in Recovery: Treatment for Opioid Use Disorder, Planning for Success (https:// media.samhsa.gov/MAT-Decisions-in-Recovery /section/how/planning_for_success.aspx). Provides assistance in developing a recovery plan.
- Bringing Recovery Supports to Scale Technical Assistance Center Strategy (www.samhsa.gov /brss-tacs) and Shared Decision-Making Tools (www.samhsa.gov/brss-tacs/recovery-support -tools/shared-decision-making). Offers training and technical assistance on many topics related to medication for OUD, including recovery-oriented systems of care, mutual-support groups, capacity building, leadership by people in recovery and family members, certification requirements for peer specialists and mutual-support group coaches, and core competencies for recovery-oriented behavioral health workers.
- *Pharmacologic Guidelines for Treating Individuals With Post-Traumatic Stress Disorder and Co-Occurring Opioid Use Disorders* (https://store.samhsa.gov/shin /content/SMA12-4688/SMA12-4688.pdf).
- *General Principles for the Use of Pharmacological Agents To Treat Individuals With Co-Occurring Mental and Substance Use Disorders* (https://store.samhsa.gov/shin /content/SMA12-4689/SMA12-4689.pdf).

Veterans Administration (**VA)/Department of Defense** (**DoD)** ***Clinical Practice Guideline for the Management of Substance Use Disorders*** (www.healthquality.va.gov/guidelines/MH/sud /VADoDSUDCPGRevised22216.pdf): Provides information on screening, assessment, and treatment of OUD as well as other SUDs. It is primarily for VA and DoD healthcare providers and others involved in the care of service members or veterans with an SUD.

Assessment Scales and Screening Tools

AAAP, Education & Training (www.aaap.org /education-training/cme-opportunities): Provides Performance-in-Practice Clinical Modules for alcohol use disorder and tobacco use disorder.

American Psychiatric Nurses Association, Tobacco & Nicotine Use Screening Tools & Assessments (www.apna.org/i4a/pages/index .cfm?pageID=6150): Provides the Fagerström screening tools for nicotine dependence and smokeless tobacco and a screening checklist for adolescent tobacco use.

ASAM *Appropriate Use of Drug Testing in Clinical Addiction Medicine* (www.asam.org /quality-practice/guidelines-and-consensus -documents/drug-testing): Gives information on the appropriate use of drug testing in identifying, diagnosing, and treating people with or at risk for SUDs.

Clinical Institute Narcotic Assessment Scale for Withdrawal Symptoms (www.ncpoep.org /wp-content/uploads/2015/02/Appendix_7_Clinical_Institute_Narcotic_Assessment_CINA_Scale_for_Withdrawal_Symptoms.pdf).

NIDA, Screening, Assessment, and Drug Testing Resources (www.drugabuse.gov /nidamed-medical-health-professionals/tool -resources-your-practice/additional-screening -resources): Gives resources such as an evidence-based screening tool chart for adolescents and adults and drug use screening tool supports; also has a clinician resource and quick reference guide for drug screening in general medical settings.

World Health Organization *Guidelines for the Psychosocially Assisted Pharmacological Treatment of Opioid Dependence* (www.ncbi .nlm.nih.gov/books/NBK143183): Includes links to the Clinical Opiate Withdrawal Scale (www.drugabuse.gov/sites/default/fles/fles /ClinicalOpiateWithdrawalScale.pdf) and other opioid withdrawal scales from Annex 10 of the guidelines.

1. Resources for Counselors and Peer Providers

Organizations

Community Care Behavioral Health Organization (www.ccbh.com): A provider network focused on recovery that has published *Supporting Recovery From Opioid Addiction: Community Care Best Practice Guidelines for Recovery-Oriented Methadone Maintenance* (www.ccbh.com/pdfs/providers/healthchoices /bestpractice/MethadoneBestPracticeGuideline .pdf), a set of recovery-oriented practice implementation guidelines for methadone programs.

Faces & Voices of Recovery (https://facesand voicesofrecovery.org): Dedicated to organizing and mobilizing the millions of Americans in recovery from addiction to alcohol and drugs, their families and friends, and other allies into recovery community organizations and networks. Faces & Voices of Recovery promotes the right resources to recover through advocacy, education, and demonstration of the power and proof of long-term recovery.

International Association of Peer Supporters (https://inaops.org): An organization for mental health and addiction peer recovery support specialists, recovery coaches, recovery educators and trainers, administrators of consumer-operated or peer-run organizations, and others.

Medication-Assisted Recovery Services (MARS) Project (www.marsproject.org): A peer-initiated, peer-based recovery support project sponsored by NAMA Recovery that offers, among other resources, an educational video about the MARS peer support program and an online network for MARS peer support personnel:

- MARS Project Video (www.marsproject.org).
- New York State Peer Recovery Network, Peers Organizing for Results Through Advocacy and Leadership (PORTAL) (http://advocacy .marsproject.org). Created to help peers in recovery more effectively organize their communities, communicate with each other, and create a stronger voice for advocacy efforts.

Pillars of Peer Support Services (www.pillarsof peersupport.org): Develops and fosters the use of Medicaid funding to support peer recovery services in state mental health systems of care.

Recovery Community Services Program— Statewide Network (www.samhsa.gov/grants /grant-announcements/ti-14-001): A SAMHSA grant program for peer-to-peer recovery support services that help people initiate and sustain recovery from SUDs.

Publications and Other Resources

ATTC's Recovery-Oriented Methadone Maintenance (www.attcnetwork.org/userfles /fle/GreatLakes/5th%20Monograph_RM_Methadone.pdf): This guide is the most thorough document on this topic currently available and is applicable to clients receiving other medications for OUD.

Community Care Behavioral Health Organization: These publications outline phase-specific tasks and accompanying strategies for programs that serve clients who take methadone or buprenorphine:
Supporting Recovery From Opioid Addiction: Community Care Best Practice Guidelines for Recovery-Oriented Methadone Maintenance (www.williamwhitepapers.com/pr/Recovery -oriented%20Methadone%20Maintenance %20Best%20Practice%20Guidelines%20 2014%20-%20CCBHO.pdf)
Supporting Recovery From Opioid Addiction: Community Care Best Practice Guidelines for Buprenorphine and Suboxone (www.ccbh.com /pdfs/providers/healthchoices/bestpractice /Community_Care_BP_Guidelines_for_Buprenorphine_and_Suboxone.pdf)

Narcotics Anonymous (NA) (www.na.org): The organization's most recent statement on medications for treating OUD—*Narcotics Anonymous and Persons*

Receiving Medication-Assisted Treatment—is available online (www.na.org /admin/include/spaw2/uploads/pdf/pr/2306_NA_PRMAT_1021.pdf).

SAMHSA (https://store.samhsa.gov): This agency oversees medications to treat opioid addiction, including methadone, buprenorphine, and naltrexone; sets regulations; guides policy; and offers information and resources for the field. SAMHSA has many recovery-oriented publications for providers:

- *Dear Colleague Letters for Medication- Assisted Treatment Providers* (www.samhsa .gov/medication-assisted-treatment /legislation-regulations-guidelines/dear -colleague-letters). Regulations, policies, and best practices for OTPs can change; these regular communications help providers stay up to date on clinical and regulatory issues related to opioid treatment.
- *Medication-Assisted Recovery: Medication Assisted Peer Recovery Support Services Meeting Report* (www.samhsa.gov/sites /default/fles/programs_campaigns /medication_assisted/dear_colleague_letters/2015-prss-summary-report.pdf).
- *Financing Recovery Support Services: Review and Analysis of Funding Recovery Support Services and Policy Recommendations* (www .samhsa.gov/sites/default/fles/partnersfor recovery/docs/RSS_fnancing_report.pdf).
- SAMHSA's *Working Definition of Recovery* (https://store.samhsa.gov/shin/content /PEP12-RECDEF/PEP12-RECDEF.pdf).
- *Access to Recovery Approaches to Recovery- Oriented Systems of Care* (https://store .samhsa.gov/product/Access-to-Recovery -ATR-Approaches-to-Recovery-Oriented -Systems-of-Care/SMA09-4440).
- *Building Bridges—Co-Occurring Mental Illness and Addiction: Consumers and Service Providers, Policymakers, and Researchers in Dialogue* (https://store.samhsa.gov/shin /content//SMA04-3892/SMA04-3892.pdf).

Selected Papers of William L. White (www .williamwhitepapers.com): Contains papers, monographs, and presentations on recovery, including recovery-oriented methadone maintenance, methadone and anti-medication bias, discrimination

and methadone, NA and the pharmacotherapeutic treatment of OUD, and co-participation in 12-Step mutual-support groups and methadone maintenance.

2. Resources for Clients and Families

Organizations

AAOTD (www.aatod.org): Offers a variety of resources, news releases about medication for the treatment of OUD, and information about its national conferences.

Al-Anon Family Groups (www.al-anon.org): Describes group meetings where friends and family members of people with substance use issues share their experiences and learn how to apply the principles of the Al-Anon program to their individual situations. Sponsorship gives members the chance to get personal support from more experienced individuals in the program.

Alcoholics Anonymous (AA) (www.aa.org): Offers group meetings for people who have problems relating to drinking and wish to stop. AA sponsors provide members with more personal support from experienced individuals. Many people who are taking medication to treat OUD find AA increasingly receptive to their decisions about medication, and AA meetings are more widely available to these individuals.

ASAM: Provides patient and family education tools about addiction in general and OUD specifically:

- Patient Resources (www.asam.org/resources /patientresources)
- *Opioid Addiction Treatment: A Guide for Patients, Families, and Friends* (http://eguideline.guidelinecentral.com /i/706017-asam-opioid-patient-piece/0?)

Double Trouble in Recovery (www.hazelden.org /HAZ_MEDIA/3818_doubletroubleinrecovery. pdf): Describes a fellowship of people who support each other in recovering from substance use and mental disorders.

Dual Recovery Anonymous (www.draonline.org): Presents information on mutual-help organization that follows 12-Step principles in supporting people recovering from addiction and emotional or mental illness. Focuses on preventing relapse and actively improving members' quality of life through a community of mutual support.

Faces & Voices of Recovery (https://facesand voicesofrecovery.org): Offers recovery stories, news, events information, publications, and webinars.

Heroin Anonymous (http://heroinanonymous .org): Describes a nonprofit fellowship of individuals in recovery from heroin addiction committed to helping each other stay sober. This organization holds local support meetings, a directory of which can be found on its website.

LAC (https://lac.org): Offers information about the rights of people with criminal records, HIV/AIDS, and SUDs.

Learn to Cope (www.learn2cope.org): Describes a secular mutual-help group that offers education, resources, and peer support for the families of people with SUDs (although the focus is primarily on OUD). The organization maintains an online forum, but groups are only available in a few states.

NA (www.na.org): Provides a global, community-based organization with a multilingual, multicultural membership that supports addiction recovery via a 12-Step program, including regular group meeting attendance. Members hold nearly 67,000 meetings weekly in 139 countries. NA is an ongoing support network for maintaining a drug-free lifestyle. NA doesn't focus on a particular addictive substance.

NAMA Recovery (www.methadone.org): Offers an education series, provides training and certification for Certified MAT Advocates, and has local chapters and international affiliates that act to advocate for methadone patients. It has a

helpful webpage titled FAQs About Advocate Training and Certification (www.methadone.org /certifcation/faq.html).

Nar-Anon Family Groups (www.nar-anon.org): Provides group meetings where friends and family of people with drug use problems can share their experiences and learn to apply the 12-Step Nar-Anon program to their lives. Nar-Anon groups also offer more individualized support from experienced individuals in the program who act as sponsors.

National Alliance on Mental Illness (NAMI)
(www.nami.org): Describes the largest grassroots educational, peer support, and mental health advocacy organization in the United States. Founded in 1979 by a group of family members of people with mental disorders, NAMI has developed into an association of hundreds of local affiliates, state organizations, and volunteers.

Parents of Addicted Loved Ones (https:// palgroup.org): Presents a secular support group for parents who have a child with an SUD. The organization has meetings in only some states but also hosts telephone meetings.

Pills Anonymous (www.pillsanonymous.org): Offers a 12-Step mutual-support group that holds regular meetings in which individuals in recovery from addiction to pills share their experiences, build their strengths, and offer hope for recovery to one another.

Secular Organizations for Sobriety (www.sos sobriety.org): Describes a nonprofit, nonreligious network of autonomous, nonprofessional local groups that support people in achieving and maintaining abstinence from alcohol and drug addiction.

Self-Management for Addiction Recovery (SMART Recovery)
(www.smartrecovery.org): Is a self-empowering addiction recovery support

group; participants learn science-based tools for addiction recovery and have access to an international recovery community of mutual-help groups.

Stop Stigma Now (www.stopstigmanow.org): Describes an advocacy organization that works to eradicate prejudice associated with taking medication to treat OUD and offers resources and a media library.

Women for Sobriety (https://womenfor sobriety.org/beta2): Offers an abstinence-based mutual-help group that helps women find their individual paths to recovery by acknowledging the unique needs women have in recovery. This organization is not affiliated with any other recovery organization. It offers recovery tools to help women in recovery develop coping skills focused on emotional growth, spiritual growth, self-esteem, and a healthy lifestyle.

Publications and Other Resources

AAAP Patient Resources (www.aaap.org /patient-resources/helpful-links): Offers resources and publications for patients and their families.

Addiction Treatment Forum, *Narcotics Anonymous and the Pharmacotherapeutic Treatment of Opioid Addiction in the United States* (http://atforum.com/documents /2011NAandMedication-assistedTreatment.pdf): Presents William White's publication for people receiving medication for OUD that gives information on the pros and cons of 12-Step groups and how to prepare for meetings.

ASAM, Opioid Addiction Treatment: A Guide for Patients, Families, and Friends (http:// eguideline.guidelinecentral.com/i/706017-asam -opioid-patient-piece): Provides a guide about the treatment of OUD for patients, families, and friends.

HHS:

- Smokefree.gov (https://smokefree.gov). Provides useful information that helps individuals in planning and maintaining tobacco cessation.

- BeTobaccoFree.gov (https://betobaccofree .hhs.gov/health-effects/nicotine-health). Provides information for individuals struggling with nicotine addiction and links for clinicians that provide guidance on the care for patients with nicotine addiction.

LAC (https://lac.org/resources/substance-use -resources/medication-assisted-treatment -resources). Maintains a library of documents related to medication for the treatment of OUD and other resources, including an advocacy toolkit, sample support letter form, training materials, and webinars:

- *Driving on Methadone or Buprenorphine (Suboxone): DUI?* (http://lac.org/wp-content /uploads/2014/07/Driving-on-Methadone-or -Suboxone-DUI.pdf) factsheet.
- *Know Your Rights: Employment Discrimination Against People With Alcohol/Drug Histories* (https://lac.org/resources/substance-use -resources/employment-education-housing -resources/webinar-know-rights-employment -discrimination-people-alcoholdrug-histories) webinar.
- *Know Your Rights: Rights for Individuals on Medication-Assisted Treatment* (https://lac .org/wp-content/uploads/2014/12/Know Your Rts - MAT fnal 9.28.10.pdf) publication.
- *Medication-Assisted Treatment for Opioid Addiction: Myths and Facts* (http://lac.org /wp-content/uploads/2016/02/Myth-Fact -for-MAT.pdf) factsheet.

NAMA Recovery (www.methadone.org): Offers many resources and training opportunities to become a certifed advocate for pharmacotherapy for OUD and provides links to resources related to medication for the treatment of OUD.

National Council on Alcoholism and Drug Dependence's *Consumer Guide to Medication- Assisted Recovery* (www.ncadd.org/images /stories/PDF/Consumer-Guide-Medication -Assisted-Recovery.pdf).

NIAAA's Rethinking Drinking (www.rethinking drinking.niaaa.nih.gov/help-links): Provides links to patient and family education, help lines, and other recovery resources.

SAMHSA (https://store.samhsa.gov): Provides patient and family educational tools about OUD and medication treatment for OUD treatment. The resources below are available in several languages, including Spanish and Russian:

- *Decisions in Recovery: Treatment for Opioid Use Disorders* (https://store.samhsa.gov /product/Decisions-in-Recovery-Treatment -for-Opioid-Use-Disorders/SMA16-4993). Helps clients identify an appropriate path of recovery from OUD.
- *The Facts About Buprenorphine for Treatment of Opioid Addiction* (https://store.samhsa .gov/shin/content//SMA14-4442/SMA14 -4442.pdf).
- *The Facts About Naltrexone for Treatment of Opioid Addiction* (https://store.samhsa.gov /shin/content/SMA09-4444/SMA09-4444.pdf).
- *Know Your Rights: Rights for Individuals on Medication-Assisted Treatment* (https://store .samhsa.gov/product/Rights-for-Individuals -on-Medication-Assisted-Treatment /SMA09-4449).
- *Medication-Assisted Treatment for Opioid Addiction: Facts for Families and Friends* (www.ct.gov/dmhas/lib/dmhas/publications /MAT-InfoFamilyFriends.pdf).
- *What Every Individual Needs To Know About Methadone Maintenance* (https://store.samhsa .gov/product/What-Every-Individual-Needs -to-Know-About-Methadone-Maintenance /SMA06-4123).
- *What Is Substance Abuse Treatment? A Booklet for Families* (https://store.samhsa .gov/shin/content/SMA14-4126/SMA14 -4126.pdf)

3. Glossary of TIP Terminology

Abuse liability: The likelihood that a medication with central nervous system activity will cause desirable psychological effects, such as euphoria or mood changes, that promote the medication's misuse.

Addiction: As defined by ASAM,[55] "a primary, chronic disease of brain reward, motivation, memory, and related circuitry." It is 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**. The *Diagnostic and Statistical Manual of Mental Disorders,* Fifth Edition[56] (DSM-5), does not use the term for diagnostic purposes, but it commonly describes the more severe forms of opioid use disorder.

Bioavailability: Proportion of medication administered that reaches the bloodstream.

Care provider: Encompasses both **healthcare professionals** and other professionals who do not provide medical services, such as counselors or providers of supportive services. Often shortened to "provider."

Cross-tolerance: Potential for people tolerant to one opioid (e.g., heroin) to be tolerant to another (e.g., methadone).

Dissociation: Rate at which a drug uncouples from the receptor. A drug with a longer dissociation rate will have a longer duration of action than a drug with a shorter dissociation rate.

Half-life: Rate of removal of a drug from the body. One half-life removes 50 percent from the plasma. After a drug is stopped, it takes five half-lives to remove about 95 percent from the plasma. If a drug is continued at the same dose, its plasma level will continue to rise until it reaches steady state concentrations after about five half-lives.

Healthcare professionals: Physicians, nurse practitioners, physician assistants, and other medical service professionals who are eligible to prescribe medications for and treat patients with OUD. The term "**prescribers**" also refers to these healthcare professionals.

Induction: Process of initial dosing with medication for OUD treatment until the patient reaches a state of stability; also called initiation.

Intrinsic activity: The degree of receptor activation attributable to drug binding. **Full agonist, partial agonist**, and **antagonist** are terms that describe the intrinsic activity of a drug.

Maintenance treatment: Providing medications to achieve and sustain clinical remission of signs and symptoms of OUD and support the individual process of recovery without a specific endpoint (as with the typical standard of care in medical and psychiatric treatment of other chronic illnesses).

Medically supervised withdrawal (formerly called detoxification): Using an opioid agonist (or an alpha-2 adrenergic agonist if opioid agonist is not available) in tapering doses or other medications to help a patient discontinue illicit or prescription opioids.

Medical management: Process whereby healthcare professionals provide medication, basic brief supportive counseling, monitoring of drug use and medication adherence, and referrals, when necessary, to addiction counseling and other services to address the patient's medical, mental health, comorbid addiction, and psychosocial needs.

Mutual-help groups: Groups of people who work together on obtaining and maintaining recovery. Unlike peer support (e.g., the use of recovery coaches), mutual-help groups consist entirely of people who volunteer their time and typically have no official connection to treatment programs. Most are self-supporting. Although 12-Step groups such as AA and NA are the most widespread and well-researched type of mutual-help groups, other groups may be available in some areas. They range from groups affiliated with a religion or church (e.g., Celebrate Recovery, Millati Islami) to purely secular groups (e.g., SMART Recovery, Women for Sobriety).

Office-based opioid treatment (OBOT):
Providing medication for OUD in settings other than certified OTPs.

Opiates: A subclass of opioids derived from opium (e.g., morphine, codeine, thebaine).

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 that are normally stimulated by opioids. **Mu-opioid receptor full agonists** (e.g., methadone) bind to the mu-opioid receptor and produce actions similar to those produced by the endogenous opioid beta-endorphin. Increasing the dose increases the effect. **Mu-opioid receptor partial agonists** (e.g., buprenorphine) bind to the mu-opioid receptor. Unlike with full agonists, increasing their dose may not produce additional effects once they have reached their maximal effect. At low doses, partial agonists may produce effects similar to those of full agonists.

Opioid receptor antagonist: A substance that has an affinity for opioid receptors in the central nervous system without producing the physiological effects of opioid agonists. Mu-opioid receptor antagonists (e.g., naltrexone) can block the effects of exogenously administered opioids.
Opioid receptor blockade: Blunting or blocking of the euphoric effects of an opioid through opioid receptor occupancy by an opioid agonist (e.g., methadone, buprenorphine) or antagonist (e.g., naltrexone).

Opioids: All natural, synthetic, and semisynthetic substances that have effects similar to morphine. They can be used as medications having such effects (e.g., methadone, buprenorphine, oxycodone).

Opioid treatment program (OTP): An accredited treatment program with SAMHSA certification and DEA registration to administer and dispense opioid agonist medications that are approved by FDA to treat opioid addiction. Currently, these include methadone and buprenorphine products. Other pharmacotherapies, such as naltrexone, may be provided but are not subject to these regulations. OTPs must provide adequate medical, counseling, vocational, educational, and other assessment and treatment services either onsite or by referral to an outside agency or practitioner through a formal agreement.

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. Tolerance and withdrawal do not count toward the diagnosis in people experiencing these symptoms when using opioids under appropriate medical supervision. OUD covers a range of severity and replaces what the DSM-IV termed "opioid abuse" and "opioid dependence." An OUD diagnosis is applicable to a person who uses opioids and experiences at least 2 of the 11 symptoms in a 12-month period.

Peer support: The use of peer support specialists in recovery to provide nonclinical (i.e., not requiring training in diagnosis or treatment) recovery support services to individuals in recovery from addiction and to their families.

Peer support specialist: Someone in recovery who has lived experience in addiction plus skills learned in formal training. Peer support specialists may be paid professionals or volunteers. They are distinguished from members of mutual help groups because they maintain contact with treatment staff. They offer experiential knowledge that treatment staff often lack.

Prescribers: Healthcare professionals who are eligible to prescribe medications for OUD.

Psychosocial support: Ancillary services to enhance a patient's overall functioning and well-being, including recovery support services, case management, housing, employment, and educational services.

Psychosocial treatment: Interventions that seek to enhance a patient's social and mental functioning, including addiction counseling, contingency management, and mental health services.

Receptor affinity: Strength of the bond between a medication and its receptor. A medication with high mu-opioid receptor affinity requires lower concentrations to occupy the same number of mu-opioid receptors as a drug with lower mu-opioid receptor affinity. Drugs with high mu-opioid receptor affinity may displace drugs with lower affinity.

Recovery: A process of change through which individuals improve their health and wellness, live a self-directed life, and strive to reach their full potential. Even individuals with severe and chronic SUDs can, with help, overcome their SUDs and regain health and social function. Although abstinence from all substance misuse is a cardinal feature of a recovery lifestyle, it is not the only healthy, prosocial feature. Patients taking FDA-approved medication to treat OUD can be considered in recovery.

Recovery capital: The sum of the internal (e.g., motivation, self-efficacy, spirituality) and external (e.g., access to health care, employment, family support) resources that an individual can draw on to begin and sustain recovery from SUDs.

Recovery-oriented care: A service orientation that supports individuals with behavioral health conditions in a process of change through which they can 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. The TIP uses relapse to describe relapse prevention, a common treatment modality.

Remission: A medical term meaning a disappearance of signs and symptoms of the disease. 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**.

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. See also **medically supervised withdrawal**.

END OF THE COURSE!!