Medications for Opioid Use Disorder Improve Patient Outcomes

FDA-approved drugs reduce overdose risk but are often unavailable

Overview

In 2018, opioid overdoses in the United States caused one death every 11 minutes, resulting in nearly 47,000 fatalities.[1] The most effective treatments for opioid use disorder (OUD) are three medications approved by the Food and Drug Administration (FDA): methadone, buprenorphine, and naltrexone.[2] Using one of these can reduce a person's risk of illicit opioid use and fatal overdoses,[3] which underscores the need to increase access to medications for people with OUD.[4] While many people with OUD may also benefit from counseling, medications are proved to be beneficial even without such counseling services. Unfortunately, medications often are not available due to a lack of providers who can deliver these therapies, inadequate funding and reimbursement for treatment programs, and the stigma surrounding OUD that can keep people from accessing medications.[5] It is therefore critical for patients, providers, and policymakers to understand the efficacy of these medications in order to ensure that people with OUD have access to this evidence-based treatment.

OUD is a chronic medical condition caused by the recurrent use of opioids, including prescription drugs such as oxycodone and hydrocodone, and illicit substances such as heroin or fentanyl. OUD includes dysfunction of the brain's reward system, motivation, memory, and related circuitry and is manifested by individuals "pathologically pursuing reward and/or relief by substance use and other behaviors," according to the American Society of Addiction Medicine. As with other chronic, relapsing conditions, the clinical course of OUD often includes periods of exacerbation and remission that may continue throughout a person's lifetime.[6]

Access to FDA-approved medications

Methadone, buprenorphine, and naltrexone are the only FDA-approved medications to treat OUD. Under federal regulations for methadone treatment, the medication must typically be administered daily in a certified opioid treatment program (OTP) unless a patient meets program-specific criteria for take-home doses.[7] In accordance with federal law, buprenorphine may be prescribed by office-based clinicians, but they must first complete additional training and apply for a waiver.[8] Naltrexone can also be prescribed by office-based clinicians, though without the need for additional approvals. The medication effects—in addition to patient-specific factors, such as response to past treatment—guide medication treatment selection. These factors are highlighted in Table 1.

Opioid Treatment Program

An opioid treatment program (OTP) is a facility where patients can take medications under the supervision of staff and receive other care services.[9] These programs are state- and federally regulated, certified by the federal Substance Abuse and Mental Health Services Administration (SAMHSA), and registered with the Drug Enforcement Administration.[10] They can exist in a number of care settings, including intensive outpatient, residential, and hospital settings. Under existing federal regulations, OTPs are the only venue where patients can receive methadone for the treatment of opioid use disorder (OUD); some also offer buprenorphine and naltrexone.[11]

Buprenorphine Waivers

Clinicians who wish to prescribe buprenorphine for the treatment of OUD must obtain a waiver per the Drug Addiction Treatment Act of 2000.[12] Physicians must complete eight hours of SAMHSA-approved training (24 hours are required for nurse practitioners, physician assistants, and other qualified practitioners), which is available online or in person, to obtain a waiver from the DEA.[13] Once prescribers receive a waiver, they may treat a designated number of patients with approved buprenorphine products in an outpatient practice setting.

Mechanisms of action

Receptors, which are found on human cells, are places where a drug or substance made by the body binds to either cause or block an effect. Methadone and buprenorphine are opioid agonists, meaning they bind to and activate receptors on cells called mu-opioids, causing a biological response in the same way that heroin or other drugs such as oxycodone and morphine do. (See Figure 1.)

Methadone is a full agonist, meaning that it fully occupies the mu-opioid receptor. In doing so, methadone lessens the painful symptoms of opiate withdrawal and blocks the euphoric effects of other opioid drugs. Unlike heroin and other opioid agonists taken for nonmedical purposes, methadone is longer lasting, usually 24 to 36 hours, preventing the frequent peaks and valleys associated with compulsive behaviors.[14]

Buprenorphine is a partial agonist, meaning it does not completely bind to the mu-opioid receptor. As a result, buprenorphine has a ceiling effect—its effects will plateau, and will not increase even with repeated dosing. Because of this partial effect at the opioid receptor, even at high doses the risk for overdose from buprenorphine is very low.[15]

Naltrexone is an opioid antagonist, meaning that it blocks, rather than activates, the mu-opioid receptor,

preventing a biological response to block the effects of opioids if they are used. Because opioid antagonists do not produce any responses at the receptor, no physical dependence is associated with their use.[16] They are recommended for relapse prevention and for abstinence-based treatment, not for withdrawal management. Although naltrexone comes in both oral and injectable formulations, only the injectable medication is recommended for management of opioid use disorder.[17] The optimal duration of treatment for naltrexone, buprenorphine, and methadone should be patient specific with an individualized treatment plan.

Figure 1

How OUD Medications Work in the Brain

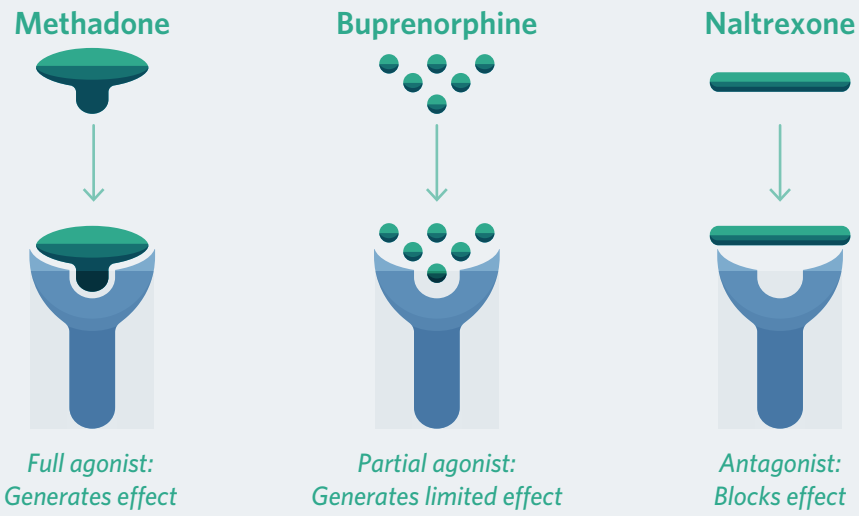

Table 1

FDA-Approved Medications to Treat OUD

Medication	Mechanism of action	Route of administration	Dosing frequency	Available through
Methadone	Full agonist	Available in pill, liquid, and wafer forms	Daily	Opioid treatment program
Buprenorphine	Partial agonist	Pill or film (placed inside the cheek or under the tongue)	Daily	Any prescriber with the appropriate waiver
		Implant (inserted beneath the skin)	Every six months	
Naltrexone	Antagonist	Oral formulations	Daily	Any health care provider with prescribing authority
		Extended-release injectable formulation	Monthly	

Source: American Society of Addiction Medicine, "The ASAM National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use" (2015), http://www.asam.org/docs/default-source/practice-support/guidelines-and-consensus-docs/asam-national-practice-guideline-supplement.pdf?sfvrsn=24

Evidence of effectiveness

Using medications to treat opioid use disorder helps people manage withdrawal symptoms, reduce illicit opioid use, and stay in treatment. Methadone and buprenorphine have also been shown to reduce the risk of death from opioid overdose. (See Table 2.) Additionally, by reducing risky behaviors such as the injection of illicit drugs, the agonist medications also decrease transmission of infectious diseases such as HIV and hepatitis C.[18] Given that all of these medications work differently and are available in different settings, the right medication will vary for each person. For example, the effectiveness of agonist medications can depend on dosing; when patients receive therapeutically effective doses of methadone and buprenorphine based on individual needs, they are better able to initiate and remain in treatment.[19]

Additionally, injectable extended-release naltrexone requires that patients detoxify before starting treatment, meaning they must abstain from opioids for seven to 14 days to rid their body of the drug.[20] This can make it more difficult for patients to initiate treatment, and leads to lower rates of treatment initiation compared with other medications.[21] Neither methadone nor buprenorphine requires detoxification, thus they are more accessible to people who are unable to stop using opioids long enough to begin naltrexone treatment. In fact, some physicians cite patient lack of interest in naltrexone, and specifically detoxification from opioids, as a barrier to prescribing the drug.[22] Furthermore, recent evidence indicates that unlike methadone and buprenorphine, naltrexone may not reduce the risk of overdose; further research is needed to resolve conflicting findings for naltrexone treatment outcomes.[23]

Table 2

Overview of OUD Medication Effectiveness

	Reduces opioid cravings	Reduces illicit opioid use	Reduces risk of opioid overdose	Increases rate of treatment retention
Methadone[24]	Yes	Yes	Yes	Yes
Buprenorphine[25]	Yes	Yes	Yes	Yes
Naltrexone[26]	Yes	Yes	Inconclusive	Yes, if initiation is possible

Note: Conclusions in the table above were drawn from a nonexhaustive review of literature on each medication compared with nonpharmacological treatment. Studies included were systematic reviews, retrospective comparative effectiveness, and randomized control trials, with more than 50 participants.

Psychosocial treatment

Psychosocial treatment, also known as behavioral health treatment, can address the behavioral health issues that often accompany OUD. While the American Society of Addiction Medicine recommends it in conjunction with all drug therapies for OUD,[27] medications are effective in treating OUD even in the absence of counseling.[28] Common therapeutic goals of psychosocial treatment are to:

- Modify underlying behaviors that may lead patients to misuse opioids.
- Encourage patients to adhere to their prescribed medications.
- Treat any other existing mental health conditions.[29]

In addition to formal behavioral health treatment, people with OUD may also benefit from nonclinical social support from peer services and mutual aid groups to encourage treatment retention and maintain recovery.[30]

Treatment gap

Despite the demonstrated effectiveness of medications used to treat opioid use disorder, many people are unable to access this treatment or have limited options for finding the medication that best meets their treatment needs. For example, as of August 2020, 43.7% of substance use treatment facilities that treat opioid use disorder do not offer any medication to treat OUD and only 4.2% offer all three medications.[31]

Two key barriers to the use of these medications are limited insurance coverage and reimbursement, and a lack of qualified medical personnel to prescribe them. Although the Affordable Care Act mandates that insurance companies pay for OUD treatment, it does not specify which benefits must be covered. Furthermore, not enough OTPs exist to meet demand for methadone treatment due to state restrictions on the number of OTPs allowed to operate and requirements for local zoning approval.[32] In fact, a majority of states have less than one OTP per 100,000 people, and between 2008 and 2018, the number of OTPs increased only incrementally, from 1,132 to 1,519.[33]

The stigma associated with people with substance use disorders and medications for OUD also plays a large role in a patient's ability to adequately access treatment.[34] This stems from the misconceptions that SUDs are moral failings instead of chronic medical conditions, and that medications substitute one drug for another. These stigmatizing beliefs can be held by the public, policymakers, medical personnel, and people with OUD. In 2018, common reasons people with OUD gave for not receiving substance use treatment included feeling that getting treatment might have a negative effect on their job (16%) and that it would cause their neighbors or community to have a negative opinion of them (15%).[35]

Conclusion

Using one of the FDA-approved medications is the most effective treatment for OUD. Because individuals vary in their treatment needs, they may need to try different approved medications to achieve their goals and may benefit from behavioral therapies as well. Improving awareness of how medications for OUD work, ensuring comprehensive coverage of all services, and expanding access to eligible providers are all integral factors in curbing the opioid epidemic.

Endnotes

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