MEDICATIONS FOR OPIOID USE DISORDER SAVE LIVES

Committee on Medication-Assisted Treatment for Opioid Use Disorder

Alan I. Leshner and Michelle Mancher, *Editors*

Board on Health Sciences Policy

Health and Medicine Division

A Consensus Study Report of

The National Academies of

SCIENCES • ENGINEERING • MEDICINE

THE NATIONAL ACADEMIES PRESS

Washington, DC

www.nap.edu

THE NATIONAL ACADEMIES PRESS 500 Fifth Street, NW Washington, DC 20001

This activity was supported by a contract between the National Academy of Sciences and the National Institutes of Health (HHSN263201800029I/HHSN26300005) and the Substance Abuse and Mental Health Services Administration. Any opinions, findings, conclusions, or recommendations expressed in this publication do not necessarily reflect the views of any organization or agency that provided support for the project.

International Standard Book Number-13: 978-0-309-48648-4
International Standard Book Number-10: 0-309-48648-3
Digital Object Identifier: https://doi.org/10.17226/25310
Library of Congress Control Number: 2019939384

Additional copies of this publication are available from the National Academies Press, 500 Fifth Street, NW, Keck 360, Washington, DC 20001; (800) 624-6242 or (202) 334-3313; http://www.nap.edu.

Printed in the United States of America

Suggested citation: National Academies of Sciences, Engineering, and Medicine. 2019. *Medications for opioid use disorder save lives*. Washington, DC: The National Academies Press. doi: https://doi.org/10.17226/25310.

Summary[1]

The opioid crisis in the United States has come about because of excessive use of these drugs for both legal and illicit purposes and unprecedented levels of consequent opioid use disorder (OUD). More than 2 million people in the United States are estimated to have OUD, which is caused by prolonged use of prescription opioids, heroin, or other illicit opioids. OUD is a life-threatening condition associated with a 20-fold greater risk of early death due to overdose, infectious diseases, trauma, and suicide. Mortality related to OUD continues to escalate as this public health crisis gains momentum across the country, with opioid overdoses killing more than 47,000 people in 2017 in the United States. Efforts to date have made no real headway in stemming this crisis, in large part because tools that already exist—like evidence-based medications—are not being deployed to maximum impact. To support the dissemination of accurate, patient-focused information about evidence-based treatment for OUD, the National Institute on Drug Abuse and the Substance Abuse and Mental Health Services Administration asked a committee convened by the National Academies of Sciences, Engineering, and Medicine to examine the evidence base for medications to treat OUD and to identify barriers that prevent people from accessing safe, effective, medication-based treatment (see Box S-1). The full Statement of Task to the committee is provided in Box S-3 at the end of this summary.

[1] This summary does not include references. Citations for the discussion presented in this summary appear in subsequent chapters.

BOX S-1
Medication-Based Treatment for Opioid Use Disorder

Although medication-assisted treatment (MAT) is a term commonly used to describe treatment programs for opioid use disorder (OUD) that include any of the three opioid agonist or antagonist medications, the committee chose to use the term "medication-based treatment for OUD" rather than MAT throughout this report. This change in nomenclature aligns with the committee's conceptual framework of OUD as a chronic disorder for which medications are first-line treatments that are often an integral part of a person's long-term treatment plan, rather than complementary or temporary aids on the path to recovery.

OUD is a chronic brain disease that comes about because of the effects of prolonged opioid use on brain structure and function. These brain changes—and the resulting addiction—can be treated with life-saving medications, but those medications are not available to most of the people who need them. Methadone, buprenorphine, and extended-release naltrexone are safe and highly effective medications that are already approved by the U.S. Food and Drug Administration (FDA) to treat OUD. By alleviating withdrawal symptoms, reducing opioid cravings, or decreasing the response to future drug use, these medications[2] make people with OUD less likely to return to drug use and risk a fatal overdose. These medications also help people restore their functionality, improve their quality of life, and reintegrate into their families and communities. These medications save lives, but the majority of people with OUD in the United States receive no treatment at all.

As with any other disease, medications should not be withheld from people with OUD without sufficient medical justification. Withholding them on ideological or other non-evidence-based grounds is denying people needed medical care. However, some addiction treatment facilities that ban medications are still being supported by funding streams that are tied to the criminal justice system or housing authorities, creating strong incentives to steer patients toward non-medication-based treatment approaches.

As the number of people with OUD surges, the need for treatment is far outstripping the current capacity to deliver it. A host of systemic barriers prevent people from accessing those medications. For example, when OUD treatment delivery settings are separate from the rest of medical care, the surrounding regulatory and legal requirements can impose hard-to-

[2] Only methadone and buprenorphine alleviate withdrawal symptoms; all three medications decrease craving and block the euphoric effects of taking other opioids.

overcome barriers on accessing medication-based treatment for OUD. The current system of care delivery for OUD is fragmented and inequitable, so a coordinated response will be required to overcome the inertia that has allowed the crisis to spiral to this extent. Box S-2 summarizes the major conclusions of the report. Curbing the epidemic will require an "all hands on deck" strategy across every sector—health care, criminal justice, patients and their family members, and beyond—because no sector alone will be able to resolve the crisis. Making access to medications much broader and more equitable is a high priority for making meaningful progress in saving lives of those with OUD.

OPIOID USE DISORDER IS A TREATABLE CHRONIC BRAIN DISEASE

Addiction is a chronic disease that involves compulsive or uncontrolled use of one or more substances in the face of negative consequences. As with other chronic medical conditions, a confluence of genetic, environmental, and social factors shape a person's vulnerability to addiction and ease of recovery from it. These factors determine a person's propensity to start using drugs and to keep using them, as well as a person's susceptibility to the particular types of neurobiological changes in the brain that characterize the progression to addiction. Building on decades of research, the scientific

BOX S-2
Summary of Conclusions

1. Opioid use disorder is a treatable chronic brain disease.
2. U.S. Food and Drug Administration (FDA)-approved medications to treat opioid use disorder are effective and save lives.
3. Long-term retention on medications to treat opioid use disorder is associated with improved outcomes.
4. A lack of availability of behavioral interventions is not a sufficient justification to withhold medications to treat opioid use disorder.
5. Most people who could benefit from medication-based treatment for opioid use disorder do not receive it, and access is inequitable across subgroups of the population.
6. Medication-based treatment is effective across all treatment settings studied to date. Withholding or failing to have available all classes of FDA-approved medication for the treatment of opioid use disorder in any care or criminal justice setting is denying appropriate medical treatment.
7. Confronting the major barriers to the use of medications to treat opioid use disorder is critical to addressing the opioid crisis.

community has coalesced around the brain disease model of addiction. In people with OUD and other substance use disorders (SUDs), prolonged and repeated drug use over time causes lasting effects on brain structure and function. Prescription and illicit opioids produce powerful and sustained effects on the brain's opioid system; repeated use can disrupt the regulation of the system and result in tolerance, physical dependence, and addiction. The evidence shows that these brain changes can be treated effectively with medications that help people refrain from using drugs, thus sharply reducing their risks of overdose and death. By alleviating opioid cravings and withdrawal symptoms, the medications can also provide opportunities to address the behavioral and social components of addiction, which are critically important both to the disorder's development and its treatment.

This scientific understanding of OUD is at odds with the prevailing public perception of the disorder, which is colored by the misconception of addiction as simply a moral failing. That popular view has proliferated through generations of social stigmatization directed at people who use drugs; this misinformed stigma has also spread to the medications used to treat OUD. In fact, people with OUD have a chronic disease that, like many others, warrants long-term medical management beyond episodic acute care incidents.

Conclusion 1:
Opioid use disorder is a treatable chronic brain disease.

OUD is a treatable chronic brain disease resulting from the changes in neural structure and function that are caused over time by repeated opioid use. The behavioral and social contexts are critically important to both its development and treatment. Stopping opioid misuse is extremely difficult. Medications are intended to normalize brain structure and function.

MEDICATIONS FOR OPIOID USE DISORDER SAVE LIVES

OUD is caused by changes in brain circuitry that can be treated with medication to restore healthy brain function, which leads to improvements in behaviors associated with addiction. The medications currently approved by FDA for treating OUD are evidence based, safe, and highly effective. Medication-based treatment for OUD focuses first on managing withdrawal symptoms and then on controlling or eliminating the patient's compulsive opioid use, most commonly with the agonist medications methadone or buprenorphine. Large systematic reviews and randomized controlled trials show that patients with OUD who receive these medications are less likely to die from overdose or other causes related to their addiction. Patients who receive medication have higher treatment retention rates, better long-term treatment outcomes, and improved social functioning; they are also less likely to inject drugs or transmit infectious diseases. For patients who have gone through withdrawal from opioids for a sufficient time, extended-release naltrexone may be used for maintenance treatment. Available evidence clearly supports the use of medications and the need to expand access to medications to reduce or eliminate compulsive opioid use, to reduce the risk of premature death, and to improve the quality of life of people with OUD and their families.

Methadone, buprenorphine, and extended-release naltrexone all work by targeting the mu-opioid receptor within the opioid system. Because each medication has a distinct mechanism of action, the most appropriate medication and dosage vary across patients and may vary in the same patient over the course of treatment. The existing medications are very effective, but they are not perfect; for example, evidence gaps remain about how to choose the most effective medication for a particular patient and how best to retain people in treatment, which is itself a significant problem. Moreover, because OUD has complex behavioral and social causes and consequences, it is not yet known which behavioral interventions might be most appropriate to help restore patients to full functionality. Therefore, even though there is a need to act urgently to improve access to existing medications, innovation cannot stagnate. Research should continue to focus on developing new and better medications to treat OUD, on determining the most effective behavioral therapies to maximize outcomes, and on refining the most appropriate protocols for their effective use.

Conclusion 2: U.S. Food and Drug Administration-approved medications to treat opioid use disorder are effective and save lives.

FDA-approved medications to treat OUD—methadone, buprenorphine, and extended-release naltrexone—are effective and save lives. The most appropriate medication varies by individual and may change over time. To stem the opioid crisis, it is critical for all FDA-approved options to be available for all people with OUD. At the same time, as with all medical disorders, continued research is needed on new medications, approaches, and formulations that will expand the options for patients.

Evidence demonstrates that patients who receive longer-term treatment with medication for OUD have better treatment outcomes; they are also less likely to die from overdose if they return to use while on medication. In fact, people with OUD are up to 50 percent less likely to die when they are being treated long term with methadone or buprenorphine. Further research is needed to define an optimal treatment regimen for each of the available medications and to directly compare the effects of the three medications' long-term use. Nonetheless, in spite of the need for more research, the body of evidence amassed over the past 50 years underscores the benefits of long-term retention on medication.

Conclusion 3: Long-term retention on medication to treat opioid use disorder is associated with improved outcomes.

There is evidence that retention on medication for the long term is associated with improved outcomes and that discontinuing medication often leads to relapse and overdose. There is insufficient evidence regarding how the medications compare over the long term.

Treatment with a combination of medication and evidence-based behavioral interventions (e.g., contingency management approaches, cognitive behavioral therapy, and structured family therapy) can be effective for many people with OUD. However, little is known about which combinations of medication and behavioral interventions are most effective, which patients are most likely to benefit from behavioral interventions, and which patients may do well with medications and appropriate medical management alone. Even among patients who would benefit from the addition of behavioral interventions, it is better for them to receive medication with appropriate medical management than to have it withheld. The life-saving aspects of these medications have been established even in the absence of accompanying behavioral interventions. Given the resource limitations faced in many settings, it is critical that providers do not withhold medications from their patients just because behavioral interventions are not available.

Conclusion 4:
A lack of availability or utilization of behavioral interventions is not a sufficient justification to withhold medications to treat opioid use disorder.

Behavioral interventions, in addition to medical management, do not appear to be a necessary part of treatment in all cases. Some people may do well with medication and medical management alone. However, evidence-based behavioral interventions can be useful in engaging people with OUD in treatment, retaining them in treatment, improving their outcomes, and helping them resume a healthy functioning life. There is inadequate evidence about which behavioral interventions, when used in conjunction with medications for OUD, are most helpful for which patients, including evidence on how effective peer support is; more research is needed to address this knowledge deficit.

MEDICATIONS ARE NOT AVAILABLE TO MANY PEOPLE WHO NEED THEM

Most people with OUD in the United States do not receive any treatment at all, and those who do receive any type of treatment may wait years to do so. Of the small proportion of people who do receive treatment, just a fraction receive medication. Access to evidence-based treatment is poor across the board, but it is starkly inequitable among certain generational, racial, ethnic, social, and economic groups. Although the research is not yet

granular enough to develop tailored treatment guidelines for specific subpopulations, the available evidence supports the effectiveness of medication for treating OUD in all groups, including adolescents, pregnant women, and people with comorbidities. However, the treatment gap is exacerbated for vulnerable populations, whose members face steep barriers in accessing medications.

Conclusion 5:
Most people who could benefit from medication-based treatment for opioid use disorder do not receive it, and access is inequitable across subgroups of the population.

Available evidence suggests that medication-based treatment for OUD is highly effective across all subgroups of the population, including adolescents, older persons, pregnant women, individuals with co-occurring disorders (e.g., psychiatric disorders, SUDs, infectious diseases), and all racial, sex and gender, and socioeconomic groups. However, the nature and extent of OUD in these groups appear to vary greatly, as does access to needed medications. To more widely and equitably address the opioid crisis, additional study will be required of the significance and causes of these differences as well as of the potential need for specific medication-based treatment guidelines for subpopulations.

Access to medications for OUD remains inequitable across different treatment settings as well. In the United States, methadone can only be administered through specialty facilities known as opioid treatment programs (OTPs), even though the available evidence shows that delivering it through an office-based medical practice setting is also effective. Moreover, most residential treatment facilities do not offer medications, and if they do, they rarely offer all three medications.

Despite the large and increasing numbers of people with OUD entering the criminal justice system in the United States, evidence-based medications are often withheld or are only provided on a limited basis for medically supervised withdrawal. As a result, few people with OUD receive medication while incarcerated or under the supervision of drug courts. In addition, justice-involved people who do receive medication for OUD are often not linked with care upon release, leading to treatment discontinuation and the concomitant risks of overdose and death. Given that these medications are known to save lives, it is arguable that withholding them from persons with OUD is unethical, as withholding insulin or blood pressure medications would be.

Pharmacies, mobile medication units, community health centers, emergency departments, and other care settings provide opportunities to engage people with OUD and link them to evidence-based care. Expanding medications for OUD into a broader range of care settings would save lives and build the capacity to make real progress against the epidemic.

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

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

A number of barriers, both social and systemic, prevent people with OUD from accessing the life-saving medications they need. Making headway against the opioid crisis will require addressing barriers related to stigma and discrimination, inadequate professional education, overly stringent regulatory and legal policies, and the fragmented systems of care delivery and financing for OUD.

The stigmatization of people with OUD is a major barrier to treatment seeking and retention. Social stigma from the general public is largely

rooted in the misconception that addiction is simply the result of moral failing or a lack of self-discipline that is worthy of blame, rather than a chronic brain disease that requires medical treatment. Evidence demonstrates that social stigma contributes to public acceptance of discriminatory measures against people with OUD and to the public's willingness to accept more punitive and less evidence-based policies for confronting the epidemic. Patients with OUD also report stigmatizing attitudes from some professionals within and beyond the health sector, further undercutting access to evidence-based treatment. The medications, particularly the agonist medications, used to treat OUD are also stigmatized. This can manifest in providers' unwillingness to prescribe medications due to concerns about misuse and diversion and in the public's mistaken belief that taking medication is "just substituting one drug for another." Importantly, the rate of diversion is lower than for other prescribed medications, and it declines as the availability of medications to treat OUD increases.

Despite the mounting crisis, the health care workforce in the United States does not receive adequate, standardized education about OUD and the evidence base for medication-based treatment. This has created a shortage of providers who are knowledgeable, confident, and willing to provide medications to patients. Many rural areas are being overwhelmed by the opioid epidemic and have very few, if any, trained and licensed providers who can prescribe the medications. Misinformation and a lack of knowledge about OUD and its medications are also prevalent across the law enforcement and criminal justice systems.

Stringent laws and regulatory policies pose substantial barriers to methadone and buprenorphine access. Laws and regulatory requirements restrict outpatient methadone treatment to state- and federally certified OTPs, which is detrimental to long-term treatment adherence for many patients. Unlike methadone, buprenorphine is approved to be prescribed in office-based settings, but only by providers who undergo specialized training and obtain a waiver from the Drug Enforcement Administration. Few providers in the United States have such waivers (estimated at less than 3 percent), and additional regulations limit the number of patients that each provider can treat with medication. To compound the problem, most waivered providers prescribe buprenorphine at well below the capacity they are allowed. These policies are not supported by evidence, nor are such strict regulations imposed on access to life-saving medications for other chronic diseases.

The system of care delivery for OUD is fragmented and poorly integrated into the broader health system in the United States. Treatment settings and financing streams for SUDs are generally detached from primary care, further obstructing access to medications for OUD, especially among people with other co-occurring conditions. Many providers are reluctant to treat people with OUD because they do not receive timely and sufficient reimbursement by public and private insurance coverage, which often limits

or excludes evidence-based medication treatment services for OUD. These barriers are compounded by other restrictions, such as prior authorization policies, dose limitations or forced dose tapers, counseling requirements, and annual or lifetime limits on the amount of OUD medication a person can receive. Almost half of nonelderly adults with OUD are covered by Medicaid, which has been shown to help connect people with medication-based treatment for OUD and to improve treatment retention. However, Medicaid coverage for OUD medications varies widely by state, with some states excluding methadone and buprenorphine entirely.

Conclusion 7: Confronting the major barriers to the use of medications to treat opioid use disorder is critical to addressing the opioid crisis.

The major barriers to the use of medications for OUD include

- High levels of misunderstanding and stigma toward drug addiction, individuals with OUD, and the medications to treat it.
- Inadequate education of the professionals responsible for working with people with OUD, including treatment providers and law enforcement and other criminal justice personnel.
- Current regulations around methadone and buprenorphine, such as waiver policies, patient limits, restrictions on settings, and other policies that are not supported by evidence or employed for other medical disorders.
- The fragmented system of care for people with OUD and current financing and payment policies.

BOX S-3
Statement of Task

To support the dissemination of accurate patient-focused information about treatments for addiction, and to help provide scientific solutions to the current opioid crisis, an ad hoc committee under the auspices of the National Academies of Sciences, Engineering, and Medicine will conduct a study of the evidence base on medication-assisted treatment (MAT)[a] for opioid use disorder (OUD). Specifically, the committee will

- Review current knowledge and gaps in understanding regarding the effectiveness of MAT for treating OUD;
- Examine available evidence on the range of parameters and circumstances in which MAT can be effectively delivered (e.g., duration of treatment, populations, settings, and interventions to address social determinants of health as a component of MAT);
- Identify challenges in implementation and uptake; and
- Identify additional research needed on MAT for OUD.

Based on its review of the literature and input from the public workshop, the committee will develop a report with its findings and conclusions.

[a] See Box S-1 for an explanation of the committee's decision to not use the term MAT in this report.

STATEMENT OF TASK AND STUDY METHODOLOGY

This consensus study was carried out by the committee between October 2018 and March 2019. Study activities included a comprehensive literature review of the effectiveness of medications for OUD and the barriers people face in accessing them. The committee held a 1.5-day public workshop in Washington, DC, which was summarized in a Proceedings of a Workshop—in Brief, as well as two 2-day closed committee meetings. The Statement of Task to the committee is provided in Box S-3.