



INTRODUCTION TO MEDICATIONS FOR OPIOID USE DISORDER TREATMENT

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Medications for Opioid Use Disorder: Updated Evidence and Persistent Access Gaps

The introductory framework this course provides for understanding medications used to treat opioid use disorder — covering the public health crisis, the benefits of medication versus no treatment, and the FDA-approved options available — has been updated by landmark reviews, revised clinical practice guidelines, and access research that both validate these medications as the standard of care and document the persistent gap between what the evidence supports and what patients can actually access.

A 2026 comprehensive review published in JAMA — the most widely read general medical journal in the world — examined pharmacological interventions across opioid use disorder, opioid withdrawal, and opioid overdose. The review documented that OUD affects approximately 3.7% of U.S. adults and confirmed three FDA-approved medications: methadone, buprenorphine, and naltrexone. The most striking finding was the treatment gap: "only 25.1% of people in the US with OUD were treated with these medications in 2022." The review also documented that community-wide naloxone distribution has been associated with 25% to 46% lower community opioid overdose rates (Harris et al., 2026). For the introductory framework this course provides, the JAMA review establishes the current state of the field in a single statistic: three-quarters of Americans with opioid use disorder are not receiving the medications that reduce mortality. The medications this course introduces are not experimental — they are the established standard of care that most patients cannot access.

The evidence base for how and where these medications get started has shifted in the fentanyl era, and a 2026 multicenter randomized clinical trial published in JAMA illustrates the change. Across 29 U.S. emergency departments between 2020 and 2024, investigators randomized 1,994 adults with opioid use disorder — 76% of whom tested positive for fentanyl — to receive either a single 24-mg injection of extended-release buprenorphine or a sublingual buprenorphine starter protocol. Treatment engagement at day 7 was 40.5% for the injection arm and 38.5% for the sublingual arm, a non-significant adjusted difference of 1.6% (95% CI, -2.8% to 6.0%); engagement at 30 days was similarly matched at 43.8% versus 44.9%. Precipitated withdrawal was rare in both groups, and participants who received the injection reported lower cravings and fewer illicit opioid use days (D'Onofrio et al., 2026). For counselors supporting MOUD patients, this trial reframes where induction can happen. A single ED visit can now connect a fentanyl-using patient to a full month of buprenorphine, and both routes of administration produce comparable short-term engagement.

Induction protocols have been a longstanding access bottleneck, especially for patients using fentanyl — and a 2025 RCT published in JAMA Network Open tested whether a much shorter lead-in could safely replace the traditional multi-day sublingual taper. Across 28 treatment centers in the United States and Canada, investigators randomized 729 adults with moderate-to-severe opioid use disorder to either rapid induction (a single 4-mg dose of buprenorphine-naloxone followed by a 300-mg extended-release buprenorphine injection) or standard induction (at least seven days of sublingual buprenorphine-naloxone before the injection). Rapid induction produced 11.8% higher retention at the second monthly injection (95% credible interval, 4.3%-19.0%), and the advantage widened to 14.8% among fentanyl-positive participants. Adverse events were comparable between arms (42.6% rapid vs. 35.5% standard) (Shiwach et al., 2025). For the induction section of this course, the Shiwach trial documents a meaningful protocol change.

The clinical practice guidelines governing how these medications are prescribed were updated in a 2024 national guideline using evidence through September 2023. The guideline established that methadone and buprenorphine are "similarly effective, particularly in reducing opioid use and adverse events, and both are now considered preferred first-line treatment options." Slow-release oral morphine was positioned as a second-line alternative. Critically, the guideline stated that "psychosocial interventions can be offered as adjunctive treatment but should not be mandatory" — meaning that counseling and behavioral therapy should supplement medication, not serve as a prerequisite for receiving it. The guideline also reinforced avoiding withdrawal management as standalone therapy (Yakovenko et al., 2024). For the medication overview this course provides, the 2024 guideline updates the clinical hierarchy: methadone and buprenorphine are co-equal first-line treatments, psychosocial treatment is recommended but not required, and detoxification alone is contraindicated. Programs that require clients to complete counseling before receiving medication or that use withdrawal management as standalone treatment are operating contrary to current clinical guidelines.

Clinical guidelines now treat methadone and buprenorphine as co-equal first-line options, but a 2026 target trial emulation in PLOS Medicine identified a population where the two medications produce meaningfully different outcomes. Using Medicare claims for 49,727 adults with opioid use disorder and comorbid chronic pain — 16,174 methadone initiators treated at opioid treatment programs and 33,553 buprenorphine initiators treated in office-based settings — investigators followed patients for one year after initiation. Methadone was associated with lower pain-related hospitalization (incidence rate ratio 0.64, 95% CI 0.58-0.70) and fewer pain-related emergency department visits (IRR 0.87, 95% CI 0.82-0.92). Opioid overdose and all-cause mortality did not differ significantly between the two medications (Wei et al., 2026). For counselors working with MOUD patients, the Wei findings sharpen a clinical nuance: the choice between methadone and buprenorphine is not only about logistics and access but also about comorbidity.

The stigma this course names as a barrier is not only a public or patient-facing issue — it also lives inside the counselor workforce. A 2025 survey published in *Addiction Science & Clinical Practice* asked 271 substance use disorder counselors from 29 Philadelphia-area agencies to document the benefits and drawbacks of methadone, buprenorphine, and naltrexone, generating 1,995 coded responses. Counselors most frequently identified reduced cravings and reduced illicit drug use as the leading benefits shared across all three medications. The most frequently reported drawback, however, was a concern that certain medications could foster "long-term medication dependence" — a framing the authors note reflects a measurable gap between counselor communication and the evidence base, which treats sustained medication use as a feature rather than a failure of successful OUD treatment (Cardamone et al., 2025). For the counselor-role section this course introduces, the Cardamone data names the specific belief that most often leaks into counseling sessions.

The access barriers that prevent the 75% treatment gap from closing were documented in a 2025 study of 2,906 rural individuals seeking medication treatment for opioid use disorder. Among those seeking treatment, 28.4% could not access it. Transportation barriers were more significant for those seeking methadone (which requires daily clinic visits), while cost and provider availability proved more problematic for injectable buprenorphine users. The researchers recommended regulatory changes to expand methadone program locations and increase prescriber adoption of newer treatment formulations (Morenz et al., 2025). For the treatment access dimension this course introduces, the Morenz et al. data identifies the specific barriers that keep evidence-based medication from reaching patients: not a lack of evidence, not a lack of FDA approval, but a lack of clinics, a lack of transportation, a lack of providers,

and a lack of affordability. The medications this course describes save lives — when patients can get to them.

How long should a patient stay on medication for opioid use disorder? A 2026 retrospective cohort study in *Addiction* analyzed 32,348 veterans who initiated buprenorphine (n=19,666), methadone (n=8,675), or extended-release naltrexone (n=4,007), with roughly 226,000 person-years of pre-discontinuation follow-up and 106,000 person-years post-discontinuation. Using all-cause mortality as the primary outcome, the authors found that the largest marginal gain in 6-year survival from an additional year on MOUD occurred at approximately two years of continuous treatment. Statistically significant survival benefits continued through roughly four to five years of retention relative to the common six-month retention benchmark. The authors concluded that "quality metrics based solely on 6-month MOUD retention appear insufficient for optimizing patient outcomes" (Hayes et al., 2026). For the evidence base this course introduces, the Hayes findings challenge a widely used performance measure. Six months on medication is not a clinical finish line; it is an early checkpoint. The implication for counselors and program planners is that conversations about treatment duration should be framed around years rather than months, and that the systems and supports clients need to remain on medication beyond the first six months — stable housing, ongoing prescriber relationships, insurance continuity, and clinical care that does not pressure tapering — are themselves clinical interventions in the truest sense. When a client asks "how long do I have to be on this," the most evidence-based answer the counselor can give is that the survival benefit accrues year over year, that two years is roughly where the curve begins to flatten, and that there is no point in the available data at which staying on medication has been shown to be worse than coming off it.



Part 1: Introduction to Medications for Opioid Use Disorder Treatment *For Healthcare and Addiction Professionals, Policymakers, Patients, and Families*

Part 1 of this **Treatment Improvement Protocol (TIP)** will help readers understand key facts and issues related to providing Food and Drug Administration (FDA)-approved medications used to treat opioid use disorder (OUD).

TIP Navigation

Executive Summary

For healthcare and addiction professionals, policymakers, patients, and families

Part 1: Introduction to Medications for Opioid Use Disorder Treatment *For healthcare and addiction professionals, policymakers, patients, and families*

Part 2: Addressing Opioid Use Disorder in General Medical Settings
For healthcare professionals

Part 3: Pharmacotherapy for Opioid Use Disorder
For healthcare professionals

Part 4: Partnering Addiction Treatment Counselors With Clients and Healthcare Professionals
For healthcare and addiction professionals

Part 5: Resources Related to Medications for Opioid Use Disorder
For healthcare and addiction professionals, policymakers, patients, and families

KEY MESSAGES

- Increasing opioid overdose deaths, illicit opioid use, and prescription opioid misuse constitute a public health crisis.
- OUD medications reduce illicit opioid use, retain people in treatment, and reduce risk of opioid overdose death better than treatment with placebo or no medication.
- Only physicians, nurse practitioners, and physician assistants can prescribe buprenorphine for OUD. They must get a federal waiver to do so.
- Only federally certified, accredited opioid treatment programs (OTPs) can dispense methadone to treat OUD. OTPs can administer and dispense buprenorphine without a federal waiver.
- Any prescriber can offer naltrexone.
- OUD medication can be taken on a short- or long-term basis, including as part of medically supervised withdrawal and as maintenance treatment.
- Patients taking medication for OUD are considered to be in recovery.
- Several barriers contribute to the underuse of medication for OUD.



SAMHSA

Substance Abuse and Mental Health
Services Administration



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PART 1 of 5

Introduction to Medications for Opioid Use Disorder Treatment

Part 1 of this TIP offers a general introduction to providing medications to address opioid use disorder (OUD). It is for all audiences. Part 1 will help readers understand key facts and issues related to providing FDA-approved medications used to treat OUD. TIP Parts 2 through 5 cover these issues in more detail.

The Approach to OUD Care

According to the Substance Abuse and Mental Health Services Administration (SAMHSA) and the National Institute on Drug Abuse, addiction is a chronic, treatable illness. Opioid addiction, which generally corresponds with moderate to severe forms of OUD (Exhibit 1.1), often requires continuing care for effective treatment rather than an episodic, acute-care treatment approach.

The World Health Organization's (WHO's) principles of good care for chronic diseases can guide OUD care:¹

- Develop a treatment partnership with patients.
- Focus on patients' concerns and priorities.
- Support patient self-management of illness.
- Use the five A's at every visit (assess, advise, agree, assist, and arrange).
- Organize proactive follow-up.
- Link patients to community resources/support.
- Work as a clinical team.
- Involve "expert patients," peer educators, and support staff in the health facility.
- Ensure continuity of care.

Chronic care management is effective for many long-term medical conditions, such as diabetes and cardiovascular disease, and it can offer



Estimated cost of the **OPIOID EPIDEMIC** was **\$504 BILLION** in 2015.²

similar benefits to patients with substance use disorders (SUDs); for example, it can help them stabilize, achieve remission of symptoms, and establish and maintain recovery. Good continuing care also provides, and links to, other medical, behavioral health, and community and recovery support services.

A noticeable theme in chronic disease management is patient-centered care.

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 medications. Healthcare professionals should also make patients aware of available, appropriate recovery support and behavioral health services.



EXHIBIT 1.1. Key Terms

Addiction: As defined by the American Society of Addiction Medicine, “a primary, chronic disease of brain reward, motivation, memory, and related circuitry.”³ 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 Edition⁴ (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.⁵

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 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.⁶

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). Exhibit 1.1 defines some key terms. A full glossary is in Part 5 of this TIP.

RESOURCE ALERT

Shared Decision Making

SAMHSA's shared decision-making tool is helpful for educating patients and their families about OUD. The information this tool provides can help patients make informed decisions about their care (<http://archive.samhsa.gov/MAT-Decisions-in-Recovery/Default.aspx>).

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 naltrexone (XR-NTX), and buprenorphine were each found to be more effective in reducing illicit opioid use than no medication in randomized clinical trials,^{9,10,11,12} 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.^{13,14,15,16,17}



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 supervised withdrawal	Medically supervised withdrawal, maintenance
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 from 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 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.¹⁹

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.²⁰ 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.²¹

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.²²

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.^{23,24,25} Higher methadone doses are associated with superior outcomes.^{26,27} Given the evidence of methadone's effectiveness, WHO lists it as an essential medication.²⁸

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.^{29,30,31} Longitudinal studies have also found that it is associated with:^{32,33,34,35,36,37,38,39,40}

- 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.^{41,42,43}

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:⁴⁴

- 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 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.⁴⁶

Oral naltrexone is also available, but it has not been found to be superior to placebo or to no medication in clinical trials.⁴⁷ Nonadherence limits its use.

Buprenorphine

Buprenorphine in its sublingual form retains patients in treatment and reduces illicit opioid use more effectively than placebo.⁴⁸ It also reduces HIV risk behaviors.^{49,50} 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.⁵¹ Another randomized trial showed that continued buprenorphine also improved treatment retention and reduced illicit prescription opioid use compared with buprenorphine dose taper.⁵² Long-term studies of buprenorphine show its effectiveness outside of clinical research protocols.^{53,54} Naloxone, a short-acting opioid antagonist, 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.⁵⁵ 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 already clinically stable.⁵⁶ More research is needed to establish implants' effectiveness outside of research studies, but findings to date are promising.^{57,58}

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.

Exhibit 1.2 compares medications for OUD.



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.⁵⁹
- Counseling plus buprenorphine leads to significantly lower healthcare costs than little or no treatment among commercially insured patients with OUD.⁶⁰
- 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.⁶¹

Relatively few cost-benefit analyses have examined addiction treatment with medication separately from addiction treatment in general.⁶² 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.^{63,64}

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.

Only federally certified and accredited OTPs can dispense methadone for the treatment of OUD. Methadone is typically given orally as a liquid.⁶⁵

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 waived 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.”⁶⁶

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.

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.”^{67,68} 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.

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.⁶⁹ Longitudinal studies show that most patients who try to stop methadone treatment relapse during or after completing the taper.^{70,71} For example, in a large, population-based retrospective study, only 13 percent of patients who tapered

RESOURCE ALERT

OUD Medication Treatment Limits and Reporting Requirements

The following websites provide information about (1) the Department of Health and Human Services final rule to increase patient access to medication for OUD and (2) associated reporting requirements:

www.federalregister.gov/documents/2016/07/08/2016-16120/medication-assisted-treatment-for-opioid-use-disorders

www.samhsa.gov/sites/default/files/programs_campaigns/medication_assisted_understanding_patient-limit275.pdf



from methadone had successful outcomes (no treatment reentry, death, or opioid-related hospitalization within 18 months after taper).⁷² A clinical trial of XR-NTX versus treatment without medication also found increased risk of returning to illicit opioid use after discontinuing medication.⁷³

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.⁷⁴ 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.

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.^{75,76,77,78,79,80,81,82,83} 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.⁸⁴ 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.

Primary care physicians are on the front lines of providing office-based treatment with medication for OUD.

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.

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 General⁸⁵ 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 2013.⁸⁶ 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.⁸⁷

Sustained public health efforts are essential to address the urgent need for OUD treatment and the risk of related overdose, HIV, and hepatitis C virus epidemics. These efforts must remove barriers and increase access to OUD medication.



Resources

Patient success stories are inspirational. They highlight the power of OUD medication to help people achieve remission and recovery. See the “Patient Success Stories” section in Part 5 of this TIP.

Part 5 of this TIP also contains community resources and advocacy resources. The community resources are for OTP, addiction treatment, and office-based providers. The advocacy resources can help patients and others advocate for OUD medication for themselves and in their communities.



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This TIP has been divided into an executive summary and five parts so that you can quickly find what you want to know about medications for opioid use disorder (OUD).

ALL READERS (including healthcare and addiction professionals, policymakers, patients, and families)

- **[Executive Summary](#)**: Overview of OUD medications and other recovery supports
- **[Full TIP](#)**: Executive Summary, Parts 1–5 available as a single document
- **[Part 1](#)**: Introduction to the use and characteristics of OUD medications
- **[Part 5](#)**: Resources and key terms relating to OUD and OUD medications

HEALTHCARE PROFESSIONALS

- **[Part 2](#)**: Guidance on addressing OUD in general medical settings
- **[Part 3](#)**: Detailed guidance on OUD pharmacotherapy
- **[Part 4](#)**: Information on working with addiction professionals

ADDICTION PROFESSIONALS

- **[Part 4](#)**: Guidance on working with clients who take or may be candidates for OUD medication

SAMHSA Store Ordering Information

Order or download TIP 63 products from the SAMHSA Store at <https://store.samhsa.gov> or order by phone from 1-877-SAMHSA-7 (1-877-726-4727) (English and Español).

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Appendix A: Introduction to Medications for Opioid Use Disorder Treatment

Directions: To receive credits for this course, you are required to take a post test and receive a passing score. We have set a minimum standard of 80% as the passing score to assure the highest standard of knowledge retention and understanding. The test is comprised of multiple choice and/or true/false questions that will investigate your knowledge and understanding of the materials found in this CEU Matrix – The Institute for Addiction and Criminal Justice distance learning course.

After you complete your reading and review of this material, you will need to answer each of the test questions. Then, submit your test to us for processing. This can be done in the following manner:

Submit your test via the Internet. All of our tests are posted electronically, allowing immediate test results and quicker processing. First, you may want to answer your post test questions found at the end of this appendix. Then, return to your browser and go to the Student Center located at:

<http://www.ceumatrix.com/studentcenter>

Once there, log in as a Returning Customer using your Email Address and Password. Then click on 'View Lesson Quiz' and you will be presented with the electronic exam.

To take the exam, simply select from the choices of "a" through "e" for each multiple choice question. For true/false questions, select either "a" for true, or "b" for false. Once you are done, simply click on the submit button at the bottom of the page. Your exam will be graded and you will receive your results immediately. If your score is 80% or greater, you will receive a link to the course evaluation. You will also receive a link to the Certificate of Completion. This is the final step in the process, and you may save and / or print your Certificate of Completion.

If, however, you do not achieve a passing score of at least 80%, you will need to review the course material and return to the Student Center to resubmit your answers.

NOTE: THE EXAM QUESTIONS AND /OR ANSWERS MAY BE IN A DIFFERENT ORDER IN THE ONLINE EXAM

Answer the following questions by selecting the most appropriate response.

1. All except _____ can prescribe buprenorphine for opioid use disorder.
 - a. physician assistants
 - b. registered nurses
 - c. physicians
 - d. nurse practitioners

2. Prescribers of buprenorphine must get a federal waiver to do so.
 - a. true
 - b. false

3. Methadone can be dispensed by _____ to treat opioid use disorder.
 - a. physicians
 - b. nurse practitioners
 - c. opioid treatment programs
 - d. physician assistants
 - e. all of the above

4. Naltrexone can be offered as treatment by any prescriber.
 - a. true
 - b. false

5. According to SAMHSA and the NIDA, addiction is a/an _____ illness.
 - a. acute
 - b. untreatable
 - c. contagious
 - d. chronic

6. Using a medication in tapering doses to help a patient discontinue opioid use is referred to as:
 - a. recovery
 - b. relapse
 - c. detoxification
 - d. antagonism
 - e. alleviation

7. _____ acts by reducing or eliminating withdrawal symptoms from illicit opioids.
 - a. methadone
 - b. buprenorphine
 - c. naltrexone
 - d. a and b but not c
 - e. a, b, and c

8. The use of _____ has the largest, oldest evidence base to opioid addiction.
 - a. buprenorphine
 - b. methadone
 - c. naltrexone
 - d. extended-release naltrexone

Introduction to Medications for Opioid Use Disorder Treatment

9. Extended-release naltrexone is not as effective as buprenorphine in retaining patients in treatment and in reducing illicit opioid use.

- a. true
- b. false

10. Benefits of treatment for opioid use disorders include:

- a. improved quality of life
- b. greater earned income
- c. reduced healthcare spending
- d. decreased crime
- e. all of the above

11. Prescribers in their first year of practice can treat up to ____ patients per year with buprenorphine.

- a. 10
- b. 15
- c. 30
- d. 50
- e. 100