The ASAM

NATIONAL PRACTICE GUIDELINE

For the Treatment of Opioid Use Disorder

2020 Focused Update

ASAM American Society *of* Addiction Medicine

The ASAM National Practice Guideline 2020 Focused Update

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ASAM American Society *of* Addiction Medicine

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Abbreviations and Acronyms

AA – Alcoholics Anonymous
ACOG – American College of Obstetrics and Gynecology
ACT – Assertive Community Treatment
AIDS – Acquired Immunodeficiency Syndrome
ASAM – American Society of Addiction Medicine
CBT – Cognitive Behavioral Therapy
CDC – Centers for Disease Control and Prevention
CNS – Central Nervous System
COWS – Clinical Opioid Withdrawal Scale
DATA 2000 – Drug Addiction Treatment Act of 2000
DEA – Drug Enforcement Agency
DSM-4 – Diagnostic and Statistical Manual of Mental Disorders, 4th Edition
DSM-5 – Diagnostic and Statistical Manual of Mental Disorders, 5th Edition
ECG – Electrocardiogram
EMS – Emergency Medical Services
FDA – U.S. Food and Drug Administration
HBV – Hepatitis B Virus
HCV – Hepatitis C Virus
HIV – Human Immunodeficiency Virus
IDU – Injection Drug Use
IM – Intramuscular
IV – Intravenous
NA – Narcotics Anonymous
NAS Neonatal Absence Syndrome
NIH – National Institutes of Health
NIDA – National Institute on Drug Abuse
NIAAA – National Institute on Alcohol Abuse and Alcoholism
NOWS – Neonatal Opioid Withdrawal Syndrome
NSAIDs – Nonsteroidal Anti-inflammatory Drugs
NSDUH – National Survey on Drug Use and Health
OBOT – Office-Based Opioid Treatment
OOWS – Objective Opioid Withdrawal Scale
OTP – Opioid Treatment Program
PMDP – Prescription Drug Monitoring Program
RCT – Randomized Controlled Trial
RAM – RAND/UCLA Appropriateness Method
SAMHSA – Substance Abuse and Mental Health Services Administration
SMART – Self-Management and Recovery Therapy
SOWS – Subjective Opioid Withdrawal Scale
TB – Tuberculosis
UROD – Ultra-rapid Opioid Detoxification

National Practice Guideline Glossary

Abstinence: Intentional and consistent restraint from the pathological pursuit of reward and/or relief that involves the use of substances and other behaviors. These behaviors may involve, but are not necessarily limited to substance use, gambling, video gaming, or compulsive sexual behaviors.[1] Use of FDA approved medications for the treatment of substance use disorder is consistent with abstinence.

Abuse: This term is not recommended for use in clinical or research contexts. Harmful use of a specific psychoactive substance. When used to mean substance abuse, this term previously applied to one category of psychoactive substance-related disorders in the DSM. While recognizing that the term abuse is part of past diagnostic terminology, ASAM recommends that an alternative term be found for this purpose because of the pejorative connotations of the word abuse.

Addiction: Addiction is a treatable, chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual's life experiences. People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences. Prevention efforts and treatment approaches for addiction are generally as successful as those for other chronic diseases.

Addiction specialist clinician: A health professional involved in the assessment, diagnosis, and treatment of addiction, such as a physician, psychologist, nurse practitioners (NPs), physician assistants (PA), clinical nurse specialists, certified registered nurse anesthetists, certified nurse midwives (as distinguished from one specializing in research).

Addiction specialist physician: Addiction specialist physicians include addiction medicine physicians and addiction psychiatrists who hold either a subspecialty board certification in addiction medicine from the American Board of Preventive Medicine, a board certification in addiction medicine from the American Board of Addiction Medicine, a subspecialty board certification in addiction psychiatry from the American Board of Psychiatry and Neurology, a subspecialty board certification in addiction medicine from the American Osteopathic Association, or certification in addiction medicine from ASAM.

Adherence (see also compliance): Adherence is a term that health professionals have been using increasingly to replace the term compliance. Both terms have been used, sometimes interchangeably, to refer to how closely patients cooperate with, follow, and take personal responsibility for the implementation of their treatment plans. The terms may be narrowly applied to how well patients follow medication instructions or, more broadly, to all components of treatment. Assessment of patients' efforts to accomplish the goals of a treatment plan is essential to treatment success. These efforts occur along a complex spectrum from independent proactive commitment, to mentored collaboration, to passive cooperation, to reluctant partial agreement, to active resistance, and to full refusal. Attempts to understand factors that promote or inhibit adherence/compliance must take into account behaviors, attitudes, willingness, and varying degrees of capacity and autonomy. The term adherence emphasizes the patient's collaboration and participation in treatment. It contributes to a greater focus on motivational enhancement approaches that engage and empower patients.

Adolescence: The American Academy of Pediatrics categorizes adolescence as the totality of three developmental stages (early-, middle- and late-adolescence)—puberty to adulthood—that occur generally between 11 and 21 years of age.[1] This clinically-driven definition may differ from legal definitions.

Agonist medication: See Opioid Agonist Medication.

Antagonist medication: See Opioid Antagonist Medication.

ASAM Criteria dimensions: *The ASAM Criteria* use six dimensions to define a holistic biopsychosocial assessment of an individual to be used for service and treatment planning including: acute intoxication or withdrawal potential; biomedical conditions and complications; emotional, behavioral, or cognitive conditions or complications; readiness for change; continued use or continued problem potential; and recovery/living environment.[2]

Assertive community treatment (ACT): An evidence-based, outreach-oriented, service delivery model for people with severe and persistent mental illness(es) that uses a team-based model to provide comprehensive and flexible treatment.

Clinician: A health professional involved in the assessment, diagnosis, and treatment of medical problems, such as a physician, psychologist, nurse practitioners (NPs), physician assistants (PA), clinical nurse specialists, certified registered nurse anesthetists, certified nurse midwives (as distinguished from one specializing in research).

Cognitive behavioral therapy: An evidence-based psychosocial intervention that seeks to modify harmful beliefs and maladaptive behaviors, and help patients recognize, avoid, and cope with the situations in which they are most likely to misuse substances.

Co-occurring disorders: Concurrent substance use and physical or mental disorders. Other terms used to describe co-occurring disorders include dual diagnosis, dual disorders, concurrent disorders, coexisting disorders, comorbid disorders, and individuals with co-occurring psychiatric and substance symptomatology (ICOPSS). Use of the term carries no implication as to which disorder is primary and which secondary, which disorder occurred first, or whether one disorder caused the other.

Compliance: See also Adherence. To comply is ''to act in accordance with another's wishes, or with rules and regulations'' (Webster's Dictionary). The term compliance is falling into disuse because patient engagement and responsibility to change is a goal beyond passive compliance. Given the importance of shared decision-making to improve collaboration and outcomes, patients are encouraged to actively participate in treatment decisions and take responsibility for their treatment, rather than to passively comply.

Concomitant conditions: Medical conditions (e.g., HIV, cardiovascular disease) and/or psychiatric conditions (e.g., depression, schizophrenia) that occur along with a substance use disorder.

Contingency management: An evidence-based psychosocial intervention in which patients are given tangible rewards to reinforce positive behaviors such as treatment participation or abstinence. Also referred to as motivational incentives.

Criminal Justice System: Consists of law enforcement agencies, courts and accompanying prosecution and defense lawyers, and agencies for detaining and supervising offenders. The total correctional population is the population of persons incarcerated, either in a prison or a jail, and persons supervised in the community, either through problem solving courts or on probation or parole.

Dependence: Used in three different ways: physical dependence is a state of neurological adaptation that is manifested by a drug class-specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist; psychological dependence is a subjective sense of need for a specific psychoactive substance, either for its positive effects or to avoid negative effects associated with its abstinence; and one category of psychoactive substance use disorder in previous editions of the DSM, but not in DSM-5.[3]

Harm reduction: A treatment and prevention approach that encompasses individual and public health needs, aiming to decrease the health and socioeconomic costs and consequences of substance use and addiction-related problems, especially medical complications and transmission of infectious diseases, without necessarily requiring abstinence. A range of treatment and recovery support activities may be included in a harm reduction strategy.

Initiation (office and home): The phase of opioid use disorder treatment during which medication dosage levels are adjusted until a patient attains stabilization. Buprenorphine initiation may take place in an office-based setting or home-based setting. By regulation, methadone initiation must take place in an OTP or acute care setting (under limited circumstances).[4,5] The previous version of these guidelines used the term induction. While the meaning is the same in this context, the Guideline Committee noted that this language did not align with the terminology used for other medical conditions and can make the process sound more difficult and complex than it is.

Illicit opioid use (including nonmedical use): Use of an illicit opioid or the use of a prescribed medicine for reasons other than those intended by the prescriber, for example, to produce positive or negative reward. Nonmedical use of prescription drugs often includes use of a drug in higher doses than authorized by the prescriber or through a different route of administration than intended by the prescriber, and for a purpose other than the indication intended by the prescriber (e.g., the use of methylphenidate prescribed for attention deficit hyperactivity disorder [ADHD] to produce euphoria rather than to reduce symptoms or dysfunction from ADHD).

Maintenance medication(s): Pharmacotherapy on a consistent schedule for persons with addiction, usually with an agonist or partial agonist, which mitigates against the pathological pursuit of reward and/or relief and allows remission of overt addiction-related problems.

Maintenance medications for addiction are associated with the development of a pharmacological steady state in which receptors for addictive substances are occupied, resulting in relative or complete blockade of central nervous system receptors such that addictive substances are no longer sought for reward and/or relief. Maintenance medications for addiction are also designed to mitigate against the risk of overdose. Depending on the circumstances of a given case, maintenance medications can be temporary or can remain in place lifelong. Integration of pharmacotherapy with psychosocial treatment generally is associated with the best clinical results. Maintenance medications can be part of an individual's treatment plan in abstinence-based recovery activities or can be a part of harm reduction strategies.

Medication management: Services that focus on the appropriateness, effectiveness, and safety of medications for a given patient. These services include monitoring and evaluating the patient's response to medication (including ongoing misuse of substances); dose titration as clinically indicated; education to ensure the patient understands their treatment plan, how to take their medications, potential side effects, and the importance of adherence; and provision of recommendations for other treatment and recovery support services as indicated. These services are intended to promote ongoing engagement in treatment, optimize the patient's medication response, and prevent relapse.

Moderation management: Moderation management is a behavioral change program and national support group network for people concerned about their drinking and who desire to make positive lifestyle changes. MM empowers individuals to accept personal responsibility for choosing and maintaining their own path, whether moderation or abstinence. MM promotes early self-recognition of risky drinking behavior, when moderate drinking is a more easily achievable goal.

Motivational interviewing:

1. *Layperson's definition:* A collaborative conversation style for strengthening a person's own motivation and commitment to change.
2. *Practitioner's definition:* A person-centered counseling style for addressing the common problem of ambivalence about change.
3. *Technical definition:* A collaborative, goal-oriented style of communication with particular attention to the language of change. It is designed to strengthen personal motivation for and commitment to a specific goal by eliciting and exploring the person's own reasons for change within an atmosphere of acceptance and compassion.

Naloxone challenge: Naloxone is a short-acting opioid antagonist. Naloxone challenge is a test in which naloxone is administered to patients to evaluate their level of opioid dependence before the commencement of naltrexone pharmacotherapy.

Naltrexone-facilitated opioid withdrawal management: This is a method of withdrawal management that involves the use of multiple small doses of naltrexone, sometimes in combination with buprenorphine, over several days to manage withdrawal and facilitate the initiation of treatment with naltrexone.[4]

Narcotic drugs: Legally defined by the Controlled Substances Act in the United States since its enactment in 1970. The term narcotic is broad and can include drugs produced directly or indirectly by extraction from substances of vegetable origin, or independently by means of chemical synthesis, or by a combination of extraction and chemical synthesis. The main compounds defined as narcotics in the United States include: opium, opiates, derivatives of opium and opiates, including their isomers, esters, ethers, salts, and salts of isomers, esters, ethers (but not the isoquinoline alkaloids of opium), poppy straw and concentrate of poppy straw, coca leaves, cocaine, its salts, optical and geometric isomers, and salts of isomers and ecgonine, its derivatives, their salts, isomers, and salts of isomers. Any compound, mixture, or preparation which contains any quantity of any of the substances referred to above.

Neuroadaptation: See Tolerance for the definition.

Office-based opioid treatment (OBOT): Clinicians in private practices or several types of public sector clinics that can be authorized to prescribe the partial opioid agonist buprenorphine in outpatient settings. There is no regulation, *per se,* of the clinic site itself, but of the individual clinician who prescribes buprenorphine.

Opiate: One of a group of alkaloids derived from the opium poppy *(Papaver somniferum)*, with the ability to induce analgesia, euphoria, and, in higher doses, stupor, coma, and respiratory depression. The term excludes synthetic opioids.

Opioid: A current term for any psychoactive chemical that resembles morphine in pharmacological effects, including opiates and synthetic/semisynthetic agents that exert their effects by binding to highly selective receptors in the brain where morphine and endogenous opioids affect their actions.

Opioid agonist medication: Opioid agonist medications pharmacologically occupy and activate opioid receptors in the body. They thereby relieve withdrawal symptoms and reduce or extinguish cravings for opioids.

Opioid antagonist medication: Opioid antagonist medications pharmacologically occupy opioid receptors, but do not activate the receptors. This effectively blocks the receptor, preventing the brain from responding to other opioids. The result is that further use of opioids does not produce analgesia, euphoria or intoxication.[1]

Opioid intoxication: A condition that may follow the administration of opioids, resulting in disturbances in the level of consciousness, cognition, perception, judgment, affect, behavior, or other psychophysiological functions and responses. These disturbances are related to the acute pharmacological effects of, and learned responses to, opioids. With time, these disturbances resolve, resulting in complete recovery, except when tissue damage or other complications have arisen. Intoxication depends on the type and dose of opioid and is influenced by factors such as an individual's level of tolerance. Individuals often take drugs in the quantity required to achieve a desired degree of intoxication. Behavior resulting from a given level of intoxication is strongly influenced by cultural and personal expectations about the effects of the drug. According to the International Classifications of Diseases-10 (ICD-10), acute intoxication is the term used for intoxication of clinical significance (F11.0). Complications may include trauma, inhalation of vomitus, delirium, coma, and convulsions, depending on the substance and method of administration.

Opioid treatment program (OTP): A program certified by the United States, Substance Abuse and Mental Health Services Administration (SAMHSA), to treat patients with opioid use disorder using methadone. There programs may also offer treatment with buprenorphine and/or naltrexone. An OTP can exist in several settings including, but not limited to, intensive outpatient, residential, and hospital settings. Services may include medically supervised withdrawal and/or maintenance treatment, along with various levels of medical, psychiatric, psychosocial, and other types of supportive care.

Opioid treatment services: An umbrella term that encompass a variety of pharmacological and nonpharmacological treatment modalities. This term broadens understanding of opioid treatments to include all medications used to treat opioid use disorders and the psychosocial treatment that is offered concurrently with these pharmacotherapies. Pharmacological agents include opioid agonist medications such as methadone and buprenorphine, and opioid antagonist medications such as naltrexone.

Opioid use disorder: A substance use disorder involving opioids. See Substance Use Disorder.

Opioid withdrawal management: Usually used to refer to a process of withdrawing a person from a specific psychoactive substance in a safe and effective manner. The term encompasses safe management of intoxication states (more literally, detoxification) and of withdrawal states. In this document, the term detoxification has been replaced by the term withdrawal management.[2]

Opioid withdrawal: Over time, opioids induce tolerance and neuroadaptive changes that are responsible for rebound hyperexcitability when the drug is withdrawn. The withdrawal syndrome includes craving, anxiety, dysphoria, yawning, sweating, piloerection (gooseflesh), lacrimation (excessive tear formation), rhinorrhea (running nose), insomnia, nausea or vomiting, diarrhea, cramps, muscle aches, and fever. With short-acting drugs, such as morphine or heroin, withdrawal symptoms may appear within 8–12 hours of the last dose of the drug, reach a peak at 48–72 hours, and clear after 7–10 days. With longer-acting drugs, such as methadone, onset of withdrawal symptoms may not occur until 1–3 days after the last dose; symptoms peak between the third and eighth day and may persist for several weeks.

Overdose: The inadvertent or deliberate consumption of a dose much larger than that either habitually used by the individual or ordinarily used for treatment of an illness, that results in a serious toxic reaction or death.

Patient: As used in this document, an individual receiving substance use disorder treatment. The terms client and patient sometimes are used interchangeably, although staff in nonmedical settings more commonly refer to clients.

Physical dependence: State of physical adaptation that is manifested by a drug class-specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, and/or decreasing blood level of a substance and/or administration of an antagonist.

Psychosocial interventions: Nonpharmacological interventions that may include structured, professionally administered interventions (e.g., cognitive behavior therapy or insight-oriented psychotherapy) or nonprofessional interventions (e.g., self-help groups and non-pharmacological interventions from traditional healers).

Psychosocial treatment: Any nonpharmacological. professionally administered interventions (e.g., cognitive behavior therapy or insight-oriented psychotherapy) carried out in a therapeutic context at an individual, family, or group level.

Precipitated withdrawal: A condition that occurs when an opioid agonist is displaced from the opioid receptors by an antagonist in an opioid dependent individual. It is also possible for a partial agonist to precipitate withdrawal.

Recovery: A process of sustained action that addresses the biological, psychological, social, and spiritual disturbances inherent in addiction. This effort is in the direction of a consistent pursuit of abstinence, addressing impairment in behavioral control, dealing with cravings, recognizing problems in one's behaviors and interpersonal relationships, and dealing more effectively with emotional responses. Recovery actions lead to reversal of negative, self-defeating internal processes and behaviors, allowing healing of relationships with self and others. The concepts of humility, acceptance, and surrender are useful in this process. (Note: ASAM continues to explore, as an evolving process, improved ways to define recovery.)

Remission: A state associated with an abatement of signs and symptoms that characterize active addiction. Many individuals in a remission state remain actively engaged in the process of recovery. Reduction in signs or symptoms constitutes improvement in a disease state, but remission involves a return to a level of functioning that is free of active symptoms and/or is marked by stability in the chronic signs and symptoms that characterize active addiction.

Relapse: A process in which an individual who has established disease remission experiences recurrence of signs and symptoms of active addiction, often including resumption of the pathological pursuit of reward and/or relief through the use of substances and other behaviors. When in relapse, there is often disengagement from recovery activities. Relapse can be triggered by exposure to rewarding substances and behaviors, by exposure to environmental cues to use, and by exposure to emotional stressors that trigger heightened activity in brain stress circuits. The event of using substances

or re-engaging in addictive behaviors is the latter part of the process, which can be prevented by early intervention.

Sedative, hypnotic, or anxiolytics: This class of substances includes all prescription sleeping medications and most prescription antianxiety medications (e.g. benzodiazepines, Z-medications, and gabapentinoids). Nonbenzodiazepine antianxiety medications, such as buspirone and gepirone, are not included in this class because they are not associated with significant misuse.

Sobriety: A state of sustained abstinence with a clear commitment to and active seeking of balance in the biological, psychological, social, and spiritual aspects of an individual's health and wellness that were previously compromised by active addiction.

Spontaneous withdrawal: A condition that occurs when an individual who is physically dependent on an opioid agonist suddenly discontinues or markedly decreases opioid use.

Stabilization: Attainment of a medically stable, steady state in which the patient is adequately supported to prevent deterioration of their illness.

Substance use disorder: Substance use disorder is marked by a cluster of cognitive, behavioral, and physiological symptoms indicating that the individual continues to use alcohol, nicotine, and/or other drugs despite significant related problems. Diagnostic criteria are given in the DSM-5.[5] Substance use disorder is the new nomenclature for what was included as substance dependence and substance abuse in the DSM-4.[6]

Tolerance: A decrease in response to a drug dose that occurs with continued use. If an individual is tolerant to a drug, increased doses are required to achieve the effects originally produced by lower doses. Both physiological and psychosocial factors may contribute to the development of tolerance. Physiological factors include metabolic and functional tolerance. In metabolic tolerance, the body can eliminate the substance more readily, because the substance is metabolized at an increased rate. In functional tolerance, the central nervous system is less sensitive to the substance. An example of a psychosocial factor contributing to tolerance is behavioral tolerance, when learning or altered environmental constraints change the effect of the drug. Acute tolerance refers to rapid, temporary accommodation to the effect of a substance after a single dose. Reverse tolerance, also known as sensitization, refers to a condition in which the response to a substance increased with repeated use. Tolerance is one of the criteria of the dependence syndrome.

Withdrawal management: Withdrawal management describes services to assist a patient's withdrawal. The liver detoxifies, but clinicians manage withdrawal.

EXECUTIVE SUMMARY

Purpose

The American Society of Addiction Medicine (ASAM) developed this *National Practice Guideline for the Treatment of Opioid Use Disorder* to provide information on evidence-based treatment of opioid use disorder. (Hereafter, in this document, this National Practice Guideline will be referred to as *Practice Guideline*.) This guideline is an update and replacement of the 2015 ASAM National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use.[7]

Background Updated

Opioid use disorder is a brain disorder that can range in severity from mild to severe. Diagnosis of this disorder is based on a checklist of symptoms defined in the *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition* (DSM-5) developed by the American Psychiatric Association.[5]

ASAM defines addiction as "a treatable, chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual's life experiences. People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences." Addiction is a serious biopsychosocial illness, meaning that biological, psychological, and social factors can all contribute to both the development of, and recovery from, this disease. *The ASAM Criteria* (discussed in Part 1) provide a framework for assessing how diverse biopsychosocial factors contribute to an individual patient's addiction and the type and intensity of treatment needed to support their recovery.[2] ASAM views addiction as fundamentally a neurological disease involving brain reward, motivation, memory, and related circuitry, and recognizes that there are unifying features in all cases of addiction, including substance-related addiction and nonsubstance-related addiction. In this context, the preferred term by ASAM for this disorder is addiction involving opioid use.

A variety of substances commonly associated with addiction work on specific receptors and neurotransmitter systems in the nervous system. Pharmacological agents used in the treatment of addiction exert their effects via actions on specific receptors. Hence, the medications used in the treatment of addiction have efficacy based on their own molecular structure and the particular neurotransmitter receptors affected by that medication. Medications developed for the treatment of addiction involving opioid use may have benefits in the treatment of addiction involving an individual's use of other substances. For instance, naltrexone, which is approved by the U.S. Food and Drug Administration (FDA) for the treatment of opioid dependence (using DSM, 4th Edition [DSM-4] terminology), is also FDA-approved for the treatment of alcohol dependence (DSM-4).[6]

ASAM encourages clinicians, researchers, educators, and policy makers to use the term "addiction involving " regardless of whether the patient's condition at a given point in its natural history seems to more prominently involve opioid use, alcohol use, nicotine use, or engagement in addictive behaviors such as gambling. However, given the widespread North American application of the DSM's categorization of disorders, this *Practice Guideline* will, for the sake of brevity and convention, use the term opioid use disorder.

In 2018, an estimated 10.3 million people in the United States misused opioids (representing 3.7% of the population aged 12 or older), including 9.9 million people who misused pain relievers, and 808,000 who misused heroin.[8] The 2018 National Survey of Drug Use and Health (NSDUH) further found that 2.0 million persons in America met DSM-4 criteria for opioid use disorder.[8]

Opioid misuse is associated with increased morbidity and mortality. The leading causes of death in people using opioids for non-medical purposes are overdose and trauma.[9] Injection drug use (intravenous or intramuscular [IM]) increases the risk of being exposed to HIV, viral hepatitis, and other infectious agents. As a result of the opioid epidemic, drug-use associated infections, including infective endocarditis, osteomyelitis, septic arthritis, and epidural abscesses, are increasing. A statewide study in North Carolina found that drug-use associated infective endocarditis requiring hospitalization and valve surgeries increased more than 12-fold between 2007 and 2017.[10]

Scope of Guideline

This *Practice Guideline* was developed for the treatment of opioid use disorder and the prevention of opioid overdose-related deaths. The medications covered in this guideline are mainly, but not exclusively, those that have been FDA-approved for the treatment of opioid dependence (DSM-4) or opioid use disorder (DSM-5).[5,6] The most recent version, DSM-5, combined the criteria for opioid abuse and opioid dependence, from prior versions of the DSM, in its new diagnosis of opioid use disorder. Therefore, pharmacologic treatment may not be appropriate for all patients along the entire opioid use disorder continuum. In a study comparing opioid dependence from DSM-4 and opioid use disorder from DSM-5, optimal concordance occurred when four or more DSM-5 criteria were endorsed (i.e., the DSM-5 threshold for moderate opioid use disorder).[11] Other medications have been used off-label to treat opioid use disorder (clearly noted in the text); however, the Guideline Committee has not issued recommendations on the use of those medications. As a final note, whether FDA-approved or off-label, cost and/or cost-effectiveness were not considerations in the development of this *Practice Guideline*.

Intended Audience

This *Practice Guideline* is primarily intended for clinicians involved in evaluating patients and providing authorization for pharmacological treatments at any level. The intended audience falls into the broad groups of physicians; other healthcare providers (especially those with prescribing authority); medical educators and faculty for other healthcare professionals in training; and clinical care managers, including those offering utilization management services.

Qualifying Statement

This ASAM *Practice Guideline* is intended to aid clinicians in their clinical decision-making and patient management. The *Practice Guideline* strives to identify and define clinical decision-making junctures that meet the needs of *most patients* in *most circumstances*. Clinical decision-making should involve consideration of the quality and availability of expertise and services in the community wherein care is provided. The recommendations in this guideline reflect the consensus of an independent committee (see Methodology Section) convened by ASAM between September 2018 and November 2019, to oversee a focused update of this Practice Guideline. This *Practice Guideline* will be updated regularly as clinical and scientific knowledge advances.

Prescribed courses of treatment described in this *Practice Guideline* are effective only if the recommendations, as outlined, are followed. Because lack of patient understanding and adherence may adversely affect outcomes, clinicians should make every effort to promote the patient's understanding of, and adherence to, prescribed and recommended pharmacological and psychosocial treatments. Patients should be informed of the risks, benefits, and alternatives to a particular treatment, and should be an active party to shared decision-making whenever feasible.

ASAM recognizes that there are challenges to implementation of these guidelines in certain settings, particularly in relation to the availability of all FDA approved medications for the treatment of opioid use disorder and access to psychosocial treatment in various communities and settings. However, this guideline aims to set the standard for best clinical practice, providing recommendations for the appropriate care of all patients with opioid use disorder in diverse settings. In circumstances in which the *Practice Guideline* is being used as the basis for regulatory or payer decisions, improvement in quality of care should be the goal. Recommendations in this *Practice Guideline* do not supersede any Federal or state regulation.

Overview of Methodology

This *Practice Guideline* was developed using the RAND Corporation (RAND)/University of California, Los Angeles (UCLA) Appropriateness Method (RAM) a process that combines scientific evidence and clinical knowledge to determine the appropriateness of a set of clinical procedures.[12] The RAM is a deliberate approach encompassing review of existing guidelines, literature reviews, appropriateness ratings, necessity reviews, and document development. For this project, ASAM selected an independent committee to oversee guideline development, to participate in review of treatment scenarios, and to assist in writing. For the 2015 guideline development process, ASAM's then Quality Improvement Council, chaired by Margaret Jarvis, MD, oversaw the selection process for the independent development committee, referred to as the Guideline Committee.[7]

The 2015 Guideline Committee was comprised of 11 experts and researchers from multiple disciplines, medical specialties, and subspecialties, including academic research, internal medicine, family medicine, addiction medicine, addiction psychiatry, general psychiatry, obstetrics/gynecology, pharmacology, and clinical neurobiology. Physicians with both allopathic and osteopathic training were represented in the Guideline Committee. The 2015 Guideline Committee was assisted by a technical team of researchers from the Treatment Research Institute (TRI) affiliated with the University of Pennsylvania and worked under the guidance of Dr. Kyle Kampman who led the TRI team as Principal Investigator in implementing the RAM.

2019 Focused Update New

Between September 2018 and November 2019, ASAM reconvened an independent committee (see Methodology Section) to oversee a focused update of this *Practice Guideline*.[7] The purpose of the focused update was to develop new

and revised recommendations based on a targeted review of new evidence, FDA approval of new buprenorphine formulations (see Table 1) and evolving clinical practice guidance. A full update of the guideline is scheduled to begin in 2021. ASAM's Quality Improvement Council worked with a technical team from RTI International to develop and oversee the scope of work for the focused update.

The methods used to search the literature and subsequently develop guideline statements were consistent with the RAM methodology employed for the 2015 publication. Criteria for inclusion in the focused update included new evidence and guidelines that were considered a) clinically meaningful and applicable to a broad range of clinicians treating addiction involving opioid use, and b) urgently needed to ensure the guideline reflects the current state of the science for the existing recommendations, aligns with other relevant practice guidelines, and reflects newly approved medications and formulations. Relevant evidence and current practices not meeting these criteria will be reviewed and incorporated into the full update as appropriate.

TABLE 1. Buprenorphine Formulations

Generic Name	Route of Administration Dosing	Brand Names	For the Treatment of	Formulation Considerations
Buprenorphine (monoproduct)	Sublingual Tablets Daily	Generic versions available similar to Subutex±	Opioid withdrawal and opioid use disorder	Some risk for diversion or misuse; Requires daily compliance
Buprenorphine and naloxone	Sublingual tablets and film Daily	Generic versions available in addition to Suboxone, Cassipa, Zubsolv, Bunavail	Opioid withdrawal and opioid use disorder	Lower potential for misuse and diversion (compared to monoproduct); Requires daily compliance
Buprenorphine extended-release	Extended-release Injection (Monthly)	Sublocade	Moderate to severe opioid use disorder in patients who have initiated treatment with transmucosal buprenorphine followed by dose adjustment for a minimum of 7 days	No risk for patient diversion or misuse; Requires patients to be on a stable dose of transmucosal buprenorphine for at least 7 days; Monthly instead of daily medication compliance; Less fluctuation in buprenorphine levels (compared to daily doses)
Buprenorphine extended-release	Extended-release Injection (Weekly or Monthly)	Brixadi	Moderate to severe opioid use disorder in patients who have initiated treatment with a single dose of transmucosal buprenorphine or who are already being treated with buprenorphine	Tentative approval from FDA (not eligible for marketing in the U.S. until November 30, 2020). No risk for patient diversion or misuse; only a single prior dose of transmucosal buprenorphine required prior to initiation; Weekly or Monthly instead of daily medication compliance; Less fluctuation in buprenorphine levels (compared to daily doses)
Buprenorphine hydrochloride	Subcutaneous Implant (Every 6 months)	Probuphine Implant	Treatment of opioid use disorder in patients who have achieved and sustained prolonged clinical stability on low-to-moderate doses of a transmucosal buprenorphine (i.e., no more than 8 mg per day)	Requires prolonged stability on 8 mg per day or less transmucosal buprenorphine; No risk for patient diversion or misuse; Healthcare provider training required for implant insertion and removal; Insertion site should be examined one week after insertion; Implant must be removed after 6 months; Risks associated with improper insertion and removal; Currently only FDA approved for a total treatment duration of one year (one insertion per arm); Less fluctuation in buprenorphine levels (compared to daily doses)

* Some patients may experience withdrawal/cravings when switched to a different formulation.
± Subutex was discontinued.
Table content was derived from FDA labels. Labels and label updates can be accessed at https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm.

Summary of Recommendations

Part 1: Assessment and Diagnosis of Opioid Use Disorder

Assessment Recommendations

1. The first clinical priority should be given to identifying and making appropriate referral for any urgent or emergent medical or psychiatric problem(s), including drug-related impairment or overdose.
2. NEW Comprehensive assessment of the patient is critical for treatment planning. However, completion of all assessments should not delay or preclude initiating pharmacotherapy for opioid use disorder. If not completed before initiating treatment, assessments should be completed soon thereafter.
3. MINOR REVISION Completion of the patient's medical history should include screening for concomitant medical conditions, including psychiatric disorders, infectious diseases (viral hepatitis, HIV, and tuberculosis [TB]), acute trauma, and pregnancy.
4. MINOR REVISION A physical examination should be completed as a component of the comprehensive assessment process. The prescriber (the clinician authorizing the use of a medication for the treatment of opioid use disorder) should ensure that a current physical examination is contained within the patient medical record before (or soon after) a patient is started on pharmacotherapy.
5. MINOR REVISION Initial laboratory testing should include a complete blood count, liver enzyme tests, and tests for TB, hepatitis B and C, and HIV. Testing for sexually transmitted infections should be strongly considered. Hepatitis A and B vaccinations should be offered, if appropriate.
6. MINOR REVISION Women of childbearing potential should be tested for pregnancy, and all women of childbearing potential should be queried regarding methods of contraception.
7. MINOR REVISION Patients being evaluated for opioid use disorder, and/or for possible medication use in the treatment of opioid use disorder, should undergo (or have completed) an assessment of mental health status and possible psychiatric disorders (such as is outlined in *The ASAM Criteria* and *The ASAM Standards*).[2,13]
8. MINOR REVISION Opioid use disorder is often co-occurring with other substance use disorders. Evaluation of a patient with opioid use disorder should include a detailed history of other past and current substance use and substance use disorders.
9. MINOR REVISION The use of cannabis, stimulants, alcohol, and/or other addictive drugs should not be a reason to withhold or suspend opioid use disorder treatment. However, patients who are actively using substances during opioid use disorder treatment may require greater support including a more intensive level of care (see *The ASAM Criteria* and *The ASAM Standards*).[2,13]
10. MAJOR REVISION The use of benzodiazepines and other sedative-hypnotics should not be a reason to withhold or suspend treatment with methadone or buprenorphine. While the combined use of these medications increases the risk of serious side effects, the harm caused by untreated opioid use disorder can outweigh these risks. A risk-benefit analysis should be conducted, and greater support should be provided including careful medication management to reduce risks.[14]
11. MINOR REVISION A nicotine use query should be completed routinely for all patients and counseling on cessation of the use of tobacco products and electronic nicotine delivery devices (e.g. vaping) provided if indicated.
12. MINOR REVISION As part of comprehensive care the patient should receive a multidimensional assessment (as described in *The ASAM Criteria*), including an assessment of social and environmental factors to identify facilitators and barriers to addiction treatment and long-term recovery (including pharmacotherapy).[1] Addiction is a complex biopsychosocial illness, for which the use of medication(s) is only one component of comprehensive treatment.

Diagnosis Recommendations

1. MINOR REVISION Other clinicians may diagnose opioid use disorder, but confirmation of the diagnosis must be obtained by the prescriber before pharmacotherapy for opioid use disorder commences.
2. Opioid use disorder is primarily diagnosed on the basis of the history provided by the patient and a comprehensive assessment that includes a physical examination.
3. MINOR REVISION Validated clinical scales that measure withdrawal symptoms may be used to assist in the evaluation of patients with opioid use disorder.
4. MINOR REVISION Drug testing is recommended during the comprehensive assessment process, and during treatment to monitor patients for adherence to prescribed medications and use of alcohol, illicit, and controlled substances. The frequency of testing is determined by several factors including stability of the patient, type of treatment, and treatment setting. For additional information see The ASAM Appropriate Use of Drug Testing in Clinical Addiction Medicine guidance document.[15]

Part 2: Treatment Options

1. MAJOR REVISION All FDA approved medications for the treatment of opioid use disorder should be available to all patients. Clinicians should consider the patient's preferences, past treatment history, current state of illness, and treatment setting when deciding between the use of methadone, buprenorphine, and naltrexone.
2. NEW There is no recommended time limit for pharmacological treatment.
3. MAJOR REVISION Patients' psychosocial needs should be assessed, and patients should be offered or referred to psychosocial treatment based on their individual needs. However, a patient's decision to decline psychosocial treatment or the absence of available psychosocial treatment should not preclude or delay pharmacotherapy, with appropriate medication management. Motivational interviewing or enhancement can be used to

encourage patients to engage in psychosocial treatment services appropriate for addressing individual needs.

4. (MINOR REVISION) The venue in which treatment is provided should be carefully considered. Methadone can only be provided in opioid treatment programs (OTPs) and acute care settings (under limited circumstances). Buprenorphine can be prescribed by waivered clinicians in any setting, including OTPs and office based opioid treatment (OBOT) in accordance with the Federal law (21 CFR §1301.28). Naltrexone can be prescribed in any setting by any clinician with the authority to prescribe medication. Clinicians should consider a patient's psychosocial situation, co-occurring disorders, and risk of diversion when determining which treatment setting is most appropriate (see *The ASAM Criteria* for additional guidance).[1]
5. (MINOR REVISION) Patients with active co-occurring alcohol use disorder or sedative, hypnotic, or anxiolytic use disorder (or who are in treatment for a substance use disorder involving use of alcohol or other sedative drugs, including benzodiazepines or benzodiazepine receptor agonists) may need a more intensive level of care than can be provided in an office-based setting. Persons who are regularly using alcohol or other sedatives, but do not meet the criteria for diagnosis of a specific substance use disorder related to that class of drugs, should be carefully monitored.
6. (MAJOR REVISION) The prescribing of benzodiazepines or other sedative-hypnotics should be used with caution in patients who are prescribed methadone or buprenorphine for the treatment of an opioid use disorder. While the combined use of these drugs increases the risk of serious side effects, the harm caused by untreated opioid use disorder can outweigh these risks. A risk-benefit analysis should be conducted when deciding whether to co-prescribe these medications.
7. Methadone is recommended for patients who may benefit from daily dosing and supervision in an OTP, or for patients for whom buprenorphine for the treatment of opioid use disorder has been used unsuccessfully in an OTP or OBOT setting.
8. (NEW) Opioid dosing guidelines developed for chronic pain, expressed in morphine milligram equivalents (MME), are not applicable to medications for the treatment of opioid use disorders.
9. (MINOR REVISION) Oral naltrexone for the treatment of opioid use disorder is often adversely affected by poor medication adherence and should not be used except under very limited circumstances. Clinicians should reserve its use for patients who would be able to comply with special techniques to enhance their adherence, for example, observed dosing. Extended-release injectable naltrexone reduces, but does not eliminate, issues with medication adherence.
10. (MINOR REVISION) The Prescription Drug Monitoring Program (PDMP) should be checked regularly for the purpose of confirming medication adherence and to monitor for the prescribing of other controlled substances.
11. (NEW) Naloxone, for the reversal of opioid overdose, should be provided to patients being treated for, or with a history of, opioid use disorder. Patients and family members/significant others should be trained in the use of naloxone in overdose.

Part 3: Treating Opioid Withdrawal

1. (MINOR REVISION) Using methadone or buprenorphine for opioid withdrawal management is recommended over abrupt cessation of opioids. Abrupt cessation of opioids may lead to strong cravings, and/or acute withdrawal syndrome which can put the patient at risk for relapse, overdose, and overdose death.
2. (MINOR REVISION) Opioid withdrawal management (i.e. detoxification) on its own, without ongoing treatment for opioid use disorder, is not a treatment method for opioid use disorder and is not recommended. Patients should be advised about the risk of relapse and other safety concerns, including increased risk of overdose and overdose death. Ongoing maintenance medication, in combination with psychosocial treatment appropriate for the patient's needs, is the standard of care for treating opioid use disorder.
3. (MINOR REVISION) Assessment of a patient undergoing opioid withdrawal management should include a thorough medical history and physical examination, focusing on signs and symptoms associated with opioid withdrawal.
4. (MINOR REVISION) By regulation, opioid withdrawal management with methadone must be done in an OTP or an acute care setting (under limited circumstances). For patients withdrawing from short acting opioids the initial dose should typically be 20-30 mg per day and the patient may be tapered off in approximately 6-10 days.
5. (MAJOR REVISION) Opioid withdrawal management with buprenorphine should not be initiated until there are objective signs of opioid withdrawal. (See Part 3 for more information on the timing of initiating buprenorphine.) Once signs of withdrawal have been objectively confirmed, a dose of buprenorphine sufficient to suppress withdrawal symptoms is given (an initial dose of 2-4 mg titrated up as needed to suppress withdrawal symptoms).
6. (MAJOR REVISION) Alpha-2 adrenergic agonists (e.g., FDA-approved lofexidine and off-label clonidine) are safe and effective for management of opioid withdrawal. However, methadone and buprenorphine are more effective in reducing the symptoms of opioid withdrawal, in retaining patients in withdrawal management, and in supporting the completion of withdrawal management.
7. Opioid withdrawal management using ultra-rapid opioid detoxification (UROD) is not recommended due to high risk for adverse events or death. Naltrexone-facilitated opioid withdrawal management can be safe and effective but should be used only by clinicians experienced with this clinical method, and in cases in which anesthesia or conscious sedation are not employed.

Part 4: Methadone

1. (MINOR REVISION) Methadone is a recommended treatment for patients with opioid use disorder, who are able to give informed consent and have no specific contraindication for this treatment.

2. (MAJOR REVISION) The recommended initial dose of methadone ranges from 10 to 30 mg, with reassessment as clinically indicated (typically in 2 to 4 hours). Use a lower-than-usual initial dose (2.5 to 10 mg) in individuals with no or low opioid tolerance.
3. (MAJOR REVISION) Following initial withdrawal stabilization, the usual daily dose of methadone ranges from 60 to 120 mg. Some patients may respond to lower doses and some may need higher doses. Methadone titration should be individualized based on careful assessment of the patient's response and generally should not be increased every day. Typically, methadone can be increased by no more than 10 mg approximately every 5 days based on the patient's symptoms of opioid withdrawal or sedation.
4. The administration of methadone should be monitored because unsupervised administration can lead to misuse and diversion. OTP regulations require monitored medication administration until the patient's clinical response and behavior demonstrates that prescribing non-monitored doses is appropriate.
5. (MAJOR REVISION) Patients' psychosocial needs should be assessed, and patients should be offered or referred to psychosocial treatment based on their individual needs, in conjunction with methadone in the treatment of opioid use disorder. However, a patient's decision to decline psychosocial treatment or the absence of available psychosocial treatment should not preclude or delay treatment with methadone, with appropriate medication management. Motivational interviewing or enhancement can be used to encourage patients to engage in psychosocial treatment services appropriate for addressing their individual needs.
6. (MINOR REVISION) For patients who previously received methadone for the treatment of opioid use disorder, methadone should be reinstituted immediately if relapse occurs or if an assessment determines that the risk of relapse is high (unless contraindicated). Re-initiation of methadone should follow the recommendations above regarding initial dose and titration.
7. (MINOR REVISION) Strategies directed at relapse prevention are an important part of addiction treatment and should be included in any plan of care for a patient receiving opioid use disorder treatment or ongoing monitoring of the status of their disorder.
8. (MINOR REVISION) Transitioning from methadone to another medication for the treatment of opioid use disorder may be appropriate if the patient experiences dangerous or intolerable side effects or is not successful in attaining or maintaining treatment goals through the use of methadone.
9. (MINOR REVISION) Patients transitioning from methadone to buprenorphine in the treatment of opioid use disorder should ideally be on low doses of methadone before making the transition. Patients on low doses of methadone (30–40 mg per day or less) generally tolerate transition to buprenorphine with minimal discomfort, whereas patients on higher doses of methadone may experience significant discomfort in transitioning medications.
10. (MINOR REVISION) Patients transitioning from methadone to naltrexone must be completely withdrawn from methadone and other opioids, before they can receive naltrexone. The only exception would apply when an experienced clinician receives consent from the patient to embark on a plan of naltrexone-facilitated opioid withdrawal management.
11. (MINOR REVISION) There is no recommended time limit for pharmacological treatment with methadone. Patients who discontinue methadone treatment should be made aware of the risks associated with opioid overdose, and especially the increased risk of overdose death if they return to illicit opioid use. Treatment alternatives including buprenorphine (see Part 5) and naltrexone (see Part 6), as well as opioid overdose prevention with naloxone (see part 13), should be discussed with any patient choosing to discontinue treatment.

Part 5: Buprenorphine

1. (NEW) Buprenorphine is a recommended treatment for patients with opioid use disorder, who are able to give informed consent and have no specific contraindication for this treatment.
2. (MINOR REVISION) For patients who are currently opioid dependent, buprenorphine should not be initiated until there are objective signs of opioid withdrawal to reduce the risk of precipitated withdrawal. (See discussion).
3. (MAJOR REVISION) Once objective signs of withdrawal are observed, initiation of buprenorphine should start with a dose of 2–4 mg. Dosages may be increased in increments of 2–8 mg.
4. (MAJOR REVISION) The setting for initiation of buprenorphine should be carefully considered. Both office-based and home-based initiation are considered safe and effective when starting buprenorphine treatment. Clinical judgement should be used to determine the most appropriate setting for a given patient and may include consideration of the patient's past experience with buprenorphine and assessment of their ability to manage initiation at home.
5. (MAJOR REVISION) Following initiation, buprenorphine dose should be titrated to alleviate symptoms. To be effective, buprenorphine dose should be sufficient to enable patients to discontinue illicit opioid use. Evidence suggests that 16 mg per day or more may be more effective than lower doses. There is limited evidence regarding the relative efficacy of doses higher than 24 mg per day, and the use of higher doses may increase the risk of diversion.[16]
6. (NEW) The FDA recently approved several new buprenorphine formulations for treatment of opioid use disorder (see Table 1). As data regarding the effectiveness of these products are currently limited, clinicians should use these products as indicated and be mindful of emerging evidence as it becomes available.
7. (MAJOR REVISION) Patients' psychosocial needs should be assessed, and patients should be offered or referred to psychosocial treatment based on their individual needs, in conjunction with buprenorphine in the treatment of opioid use disorder. However, a patient's decision to decline psychosocial treatment or the absence

of available psychosocial treatment should not preclude or delay buprenorphine treatment, with appropriate medication management. Motivational interviewing or enhancement can be used to encourage patients to engage in psychosocial treatment services appropriate for addressing their individual needs.

8. (MINOR REVISION) Clinicians should take steps to reduce the chance of buprenorphine diversion. Recommended strategies may include frequent office visits (e.g., weekly in early treatment); drug testing, including testing for buprenorphine and metabolites; and recall visits for medication counts. Refer to *ASAM's Sample Diversion Control Policy for additional strategies to reduce the risk for diversion*.[16]
9. (MINOR REVISION) Drug testing should be used to monitor patients for adherence to buprenorphine and use of illicit and controlled substances. For additional guidance see *The ASAM Appropriate Use of Drug Testing in Clinical Addiction Medicine*.[14]
10. (MINOR REVISION) Patients should be seen frequently at the beginning of treatment until they are determined to be stable.
11. When considering a transition from buprenorphine to naltrexone, providers should note that 7–14 days should typically elapse between the last dose of buprenorphine and the start of naltrexone to ensure that the patient is not physically dependent on opioids before starting naltrexone.
12. (MINOR REVISION) When considering a transition from buprenorphine to methadone, there is no required time delay because the transition to a full mu-opioid agonist from a partial agonist does not typically result in an adverse reaction.
13. (MINOR REVISION) There is no recommended time limit for pharmacological treatment with buprenorphine. Patients who discontinue buprenorphine treatment should be made aware of the risks associated with opioid overdose, and especially the increased risk of death if they return to illicit opioid use. Treatment alternatives including methadone (see Part 4) and naltrexone (see Part 6), as well as opioid overdose prevention with naloxone (see part 13) should be discussed with any patient choosing to discontinue treatment.
14. (MINOR REVISION) Buprenorphine taper and discontinuation is a slow process and close monitoring is recommended. Buprenorphine tapering is generally accomplished over several months. Patients should be encouraged to remain in treatment for ongoing monitoring past the point of discontinuation.

Part 6: Naltrexone

1. (MAJOR REVISION) Extended-release injectable naltrexone is a recommended treatment for preventing relapse to opioid use disorder in patients who are no longer physically dependent on opioids, able to give informed consent, and have no contraindications for this treatment.
2. (MAJOR REVISION) Extended-release injectable naltrexone should generally be administered every 4 weeks by deep IM injection in the gluteal muscle at the set dosage of 380 mg per injection. Some patients, including those who metabolize naltrexone more rapidly, may benefit from dosing as frequently as every 3 weeks.
3. (MAJOR REVISION) Oral naltrexone is not recommended except under limited circumstances (see Part 6 for more details).
4. (MAJOR REVISION) Patients' psychosocial needs should be assessed, and patients should be offered or referred to psychosocial treatment based on their individual needs, in conjunction with extended-release naltrexone. A patient's decision to decline psychosocial treatment or the absence of available psychosocial treatment should not preclude or delay naltrexone treatment, with appropriate medication management. Motivational interviewing or enhancement can be used to encourage patients to engage in psychosocial treatment services appropriate for addressing their individual needs.
5. (MINOR REVISION) There is no recommended length of treatment with naltrexone. Duration depends on clinical judgment and the patient's individual circumstances. Because there is no physical dependence associated with naltrexone, it can be stopped abruptly without withdrawal symptoms.
6. (MINOR REVISION) Transitioning from naltrexone to methadone or buprenorphine should be planned, considered, and monitored. Transitioning from an antagonist such as naltrexone to a full agonist (methadone) or a partial agonist (buprenorphine) is generally less complicated than transitioning from a full or partial agonist to an antagonist because there is no physical dependence associated with antagonist treatment and thus no possibility of precipitated withdrawal. Patients being transitioned from naltrexone to buprenorphine or methadone will not have physical dependence on opioids and thus the initial doses of methadone or buprenorphine should be low. Patients should not be transitioned until a significant amount of the naltrexone is no longer in their system, about 1 day for oral naltrexone or 28 days for extended-release injectable naltrexone.
7. (MINOR REVISION) Patients who discontinue naltrexone treatment should be made aware of the increased risks associated with opioid overdose, and especially the increased risk of overdose death, if they return to illicit opioid use. Treatment alternatives including methadone (see Part 4) and buprenorphine (see Part 5), as well as overdose prevention with naloxone (see part 13) should be discussed with any patient choosing to discontinue treatment.

Part 7: Psychosocial Treatment in Conjunction with Medications for the Treatment of Opioid Use Disorder

1. (MAJOR REVISION) Patients' psychosocial needs should be assessed, and patients should be offered or referred to psychosocial treatment, based on their individual needs, in conjunction with any pharmacotherapy for the treatment of, or prevention of relapse to, opioid use disorder. However, a patient's decision to decline psychosocial treatment or the absence of available psychosocial treatment should not preclude or delay pharmacological treatment of opioid use disorder, with appropriate medication management. Motivational interviewing or enhancement can be used to encourage patients to engage in psychosocial treatment services appropriate for addressing their individual needs.

2. Treatment planning should include collaboration with qualified behavioral healthcare providers to determine the optimal type and intensity of psychosocial treatment and for renegotiation of the treatment plan for circumstances in which patients do not adhere to recommended plans for, or referrals to, psychosocial treatment.

Part 8: Special Populations: Pregnant Women

1. NEW The first priority in evaluating pregnant women for opioid use disorder should be to identify emergent or urgent medical conditions that require immediate referral for clinical evaluation.
2. MINOR REVISION Treatment with methadone or buprenorphine is recommended and should be initiated as early as possible during pregnancy.
3. MAJOR REVISION Pregnant women who are physically dependent on opioids should receive treatment using methadone or buprenorphine rather than withdrawal management or psychosocial treatment alone.
4. MAJOR REVISION A medical examination and psychosocial assessment are recommended when evaluating pregnant women for opioid use disorder. However, completion of all assessments should not delay or preclude initiating pharmacotherapy for opioid use disorder. If not completed before initiating treatment, assessments should be completed as soon as possible thereafter.
5. Obstetricians and gynecologists, and other healthcare providers that care for pregnant women, should be alert to signs and symptoms of opioid use disorder. Pregnant women with opioid use disorder are more likely to seek prenatal care late in pregnancy, miss appointments, experience poor weight gain, or exhibit signs of withdrawal or intoxication.
6. MAJOR REVISION The psychosocial needs of pregnant women being treated for opioid use disorder should be assessed and patients should be offered or referred to psychosocial treatment based on their individual needs. A woman's decision to decline psychosocial treatment or the absence of available psychosocial treatment should not preclude or delay pharmacological treatment, with appropriate medication management, during pregnancy. Motivational interviewing or enhancement can be used to encourage patients to engage in psychosocial treatment services appropriate for addressing their individual needs.
7. Counseling and testing for HIV should be provided (in accordance with state law). Tests for hepatitis B and C and liver enzymes are also suggested. Hepatitis A and B vaccinations is recommended for those whose hepatitis serology is negative.
8. MINOR REVISION Drug and alcohol testing should be used to monitor patients for adherence to medication and for use of illicit and controlled substances. This should be done with informed consent from the mother, realizing that there may be adverse legal and social consequences for substance use. State laws differ on reporting substance use during pregnancy. Laws that penalize women for substance use and for obtaining treatment serve to prevent women from obtaining prenatal care and worsen outcomes. For further clarity see The *ASAM Appropriate Use of Drug Testing in Clinical Addiction Medicine* guidance document.[14]
9. MINOR REVISION Care for pregnant women with opioid use disorder should be comanaged by a clinician experienced in obstetrical care and a clinician experienced in the treatment of opioid use disorder.
10. Hospitalization during initiation of methadone or buprenorphine may be advisable due to the potential for adverse events, especially in the third trimester.
11. MAJOR REVISION Methadone should be initiated at a dose range of 10–30 mg. Incremental doses of 5–10 mg is recommended every 3–6 hours, as needed, to treat withdrawal symptoms, to a maximum fist day dose of 30-40 mg.
12. MAJOR REVISION After initiation, clinicians should increase the methadone dose by no more than 10 mg approximately every 5 days. The goal is to maintain the lowest dose that controls withdrawal symptoms and minimizes the desire to use additional opioids.
13. MINOR REVISION Clinicians should be aware that the pharmacokinetics of methadone are affected by pregnancy. With advancing gestational age, plasma levels of methadone progressively decrease and clearance increases. Increased and/or split doses may be needed as pregnancy progresses. Twice-daily dosing is more effective and has fewer side effects than single dosing but may not be practical because methadone is typically dispensed in an OTP. After childbirth, doses may need to be adjusted (typically reduced) based on changes in weight and metabolism.
14. MAJOR REVISION If a woman becomes pregnant while she is receiving naltrexone, it may be appropriate to discontinue the medication if the patient and clinician agree that the risk of relapse is low. A decision to remain on naltrexone during pregnancy should be carefully considered by the patient and her clinician and should include a discussion on the insufficiency of research on risks (if any) of continued use of naltrexone. If the patient chooses to discontinue treatment with naltrexone and is at risk for relapse, treatment with methadone or buprenorphine should be considered.
15. MINOR REVISION Use of naloxone challenge (see glossary) to test for opioid dependence and risk of precipitated withdrawal is not recommended for pregnant women with opioid use disorder.
16. MINOR REVISION Unless otherwise contraindicated (see Part 8), mothers receiving methadone or buprenorphine for treatment of opioid use disorders should be encouraged to breastfeed.

Part 9: Special Populations: Individuals with Pain

1. MINOR REVISION For all patients with pain, it is important that the correct diagnosis is made and that pain is addressed. Alternative treatments including non-opioid medications with pain modulating properties, behavioral approaches, physical therapy, and procedural approaches (e.g., regional anesthesia) should be considered before prescribing opioid medications for pain.

2. (MINOR REVISION) If pharmacological treatment is considered, non-opioid analgesics, such as acetaminophen and NSAIDs, and non-opioid medications with pain modulating properties should be tried first.
3. (MINOR REVISION) For patients with pain who have an active opioid use disorder but are not in treatment, methadone or buprenorphine should be considered. The patient's opioid use disorder and pain should be stabilized and managed concurrently.
4. (MAJOR REVISION) For patients taking methadone or buprenorphine for the treatment of opioid use disorder, temporarily increasing the dose or dosing frequency (i.e. split dosing to maximize the analgesic properties of these medications) may be effective for managing pain. (Titration of methadone should follow the guidance in Part 4 of this guideline)
5. (MAJOR REVISION) For patients taking methadone for the treatment of opioid use disorder who have acute pain refractory to other treatments and require additional opioid-based analgesia, adding a short acting full agonist opioid to their regular dose of methadone can be considered to manage moderate to severe acute pain. The dose of additional full agonist opioid analgesic prescribed is anticipated to be higher than the typical dose necessary to achieve adequate analgesia in opioid-naïve individuals.
6. (NEW) Patients receiving buprenorphine for opioid use disorder who have moderate to severe acute pain refractory to other treatments and require additional opioid-based analgesia may benefit from the addition of as-needed doses of buprenorphine.
7. (MAJOR REVISION) The addition of a short-acting full agonist opioid to the patient's regular dose of buprenorphine can be effective for the management of severe acute pain in supervised settings, such as during hospitalization. The dose of additional full agonist opioid analgesic prescribed is anticipated to be higher than the typical dose necessary to achieve adequate analgesia in opioid-naïve individuals. Because of a lack of evidence, the committee was unable to come to consensus on whether this adjunct treatment can be safely prescribed in ambulatory care settings.
8. (MAJOR REVISION) Discontinuation of methadone or buprenorphine before surgery is not required. Higher-potency intravenous full agonists opioids can be used perioperatively for analgesia.
9. (MINOR REVISION) Decisions related to discontinuing or adjusting the dose of buprenorphine prior to a planned surgery should be made on an individual basis, through consultation between the surgical and anesthesia teams and the addiction treatment provider when possible.
10. (MAJOR REVISION) If it is decided that buprenorphine or methadone should be discontinued before a planned surgery, this may occur the day before or the day of surgery, based on surgical and anesthesia team recommendations. Higher-potency intravenous full agonists opioids can be used perioperatively for analgesia. Methadone or buprenorphine can be resumed post-operatively when the need for full opioid agonist analgesia has resolved, with additional considerations for post-operative pain management as described for acute pain above. The initial dose and titration should typically be determined by the prescriber. In general, pre-surgery daily doses of these medications can be resumed if they were withheld for less than 2-3 days.
11. (MINOR REVISION) Patients on naltrexone may not respond to opioid analgesics in the usual manner. Therefore, it is recommended that mild pain be treated with non-opioid analgesics, and moderate to severe pain be treated with higher potency NSAIDs (e.g. ketorolac) on a short-term basis.
12. (MINOR REVISION) Oral naltrexone should be discontinued 72 hours before surgery and extended-release injectable naltrexone should be discontinued 30 days before an anticipated surgery. (Reinitiation of naltrexone should follow the guidance in Part 6 of this guideline)
13. (NEW) Naltrexone's blockade of the mu opioid receptor can often be overcome when necessary with high potency full agonist opioids. In these instances, patients should be closely monitored in an emergency department or hospital setting.

Part 10: Special Populations: Adolescents

1. Clinicians should consider treating adolescents who have opioid use disorder using the full range of treatment options, including pharmacotherapy.
2. (MINOR REVISION) Opioid agonists (methadone and buprenorphine) and antagonists (naltrexone) may be considered for treatment of opioid use disorder in adolescents. Federal laws and FDA approvals should be considered when recommending pharmacotherapy for adolescent patients.
3. (MAJOR REVISION) Psychosocial treatment is recommended in the treatment of adolescents with opioid use disorder. The risk benefit balance of pharmacological treatment without concurrent psychosocial treatment should be carefully considered and discussed with the patient and her or his parent or guardian as appropriate. A patient's decision to decline psychosocial treatment or the absence of available psychosocial treatment should not preclude or delay pharmacological treatment of opioid use disorder, with appropriate medication management. Motivational interviewing or enhancement can be used to encourage patients to engage in psychosocial treatment services appropriate for addressing their individual needs.
4. (MINOR REVISION) Concurrent practices to reduce infection (e.g., risk behavior reduction interventions) are recommended as components of comprehensive treatment for the prevention of blood-borne viruses (infections related to injection practices) and sexually transmitted infections.
5. Adolescents may benefit from treatment in specialized treatment programs that provide multidimensional services (See *The ASAM Criteria* guidelines).[2]

Part 11: Special Populations: Individuals with Co-occurring Psychiatric Disorders

1. (MINOR REVISION) A comprehensive assessment including determination of mental health status and suicide risk should be used to evaluate whether the patient is stable. Patients with suicidal or homicidal ideation should be referred immediately for treatment and possibly hospitalization.