

Executive Summary of the Focused Update of the ASAM National Practice Guideline for the Treatment of Opioid Use Disorder

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A Focused Update of the ASAM National Practice Guideline for the Treatment of Opioid Use Disorder is published in the current issue of the *Journal of Addiction Medicine*. The focused update included a search of Medline's PubMed database from January 1, 2014 to September 27, 2018, as well as a search of the grey literature (archives of the Clinical Guideline Clearinghouse, and key agency and society websites) for new practice guidelines and relevant systematic reviews addressing the use of medications and psychosocial treatments in the treatment of opioid use disorder, including within special populations. The search identified 13 practice guidelines and 35 systematic reviews that informed the subsequent RAND/UCLA Appropriateness Method (RAM) process employed to facilitate the focused update by a National Guideline Committee of addiction experts. New and updated recommendations were included if they 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 Practice 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.

Key Words: addiction, addiction medicine, addiction treatment, American Society of Addiction Medicine, ASAM, buprenorphine, clinical practice guideline, criminal justice, Methadone, Naloxone, naltrexone, opioid, opioid use disorder, opioid use disorder treatment, opioids, pain, pregnancy, substance use disorder, withdrawal

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RATIONALE

In 2015, The American Society of Addiction Medicine (ASAM) published a National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use.¹ The Practice Guideline contains recommendations for the evaluation and treatment of opioid use disorder, opioid withdrawal management, psychosocial treatment, special populations, and opioid overdose. Between September 2018 and July 2019, ASAM reconvened an independent committee to oversee a focused update of this Practice Guideline. The purpose of the focused update was to develop new and revised recommendations based on a targeted review of new evidence and evolving clinical practice guidance. 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.

GUIDELINE FOCUS

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)² or opioid use disorder (DSM-5).³ 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 (ie, the DSM-5 threshold for moderate opioid use disorder).³ 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.

TARGET POPULATIONS

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

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 currently eligible for marketing in the U.S. because of exclusivity considerations). 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; Physician 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>.

authority); medical educators and faculty for other healthcare professionals in training; and clinical care managers, including those offering utilization management services.

GUIDELINE DEVELOPMENT PROCESS

This *Practice Guideline* was developed using the RAND Corporation (RAND)/University of California, Los Angeles (UCLA) Appropriateness Method (RAM)⁴ a process that combines scientific evidence and clinical knowledge to determine the appropriateness of a set of clinical procedures. The RAM Process 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 2019 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.

EVIDENCE REVIEW AND GRADING

For the focused update, a search of Medline's PubMed database from January 1, 2014 to September 27, 2018 was conducted to identify new practice guidelines and relevant systematic reviews addressing the use of medications and psychosocial treatments in the treatment of opioid use disorder, including in special populations. The archives of the Clinical Guideline Clearinghouse, and key agency and society websites were also searched for additional newly published guidelines. The US FDA website was searched for recent relevant drug approvals and mandated label changes. A predefined set of inclusion and exclusion criteria were applied to identify practice guidelines and systematic reviews for inclusion in the Focused Update. Included guidelines and systematic reviews were not independently (ie, outside of what was performed by the publication authors) assessed for risk of bias.

The literature search identified 210 unique practice guidelines and systematic reviews. Following dual review of titles and abstracts, 67 publications were retrieved for full-text review. Of these, 11 practice guidelines⁵⁻¹⁵ and 35

systematic reviews^{16–50} met criteria for inclusion in the focused update. Key findings from included guidelines, systematic reviews and newly approved US FDA drugs, formulations and mandated label changes were abstracted and mapped to the existing ASAM recommendation statements. Using the RAM Process, hypothetical statements (ie, draft clinical guidance) were developed and presented, along with supporting evidence, to the focused update Practice Guideline Committee first for appropriateness rating and later, following revision, for necessity rating. Thirty statements were generated for the first round of appropriateness rating. Following round one, statements were revised, and 24 were presented for a second round of appropriateness and then necessity rating. The 24 newly generated statements for the focused update along with a review of the language in existing statements resulted in 35 major revisions; 57 statements underwent minor edits and the addition of 10 new recommendations. In addition, 34 statements underwent minor edits that did not change the substantive meaning of the original recommendation.

For the purposes of this document, a clinician is 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).⁵

Summary of Recommendations Updated

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*⁵¹ and *The ASAM Standards*⁵²).
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*⁵¹ and *The ASAM Standards*⁵²).
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.⁵³
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 (eg, 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*⁵¹), including an assessment of social and environmental factors to identify facilitators and barriers to addiction treatment and long-term recovery (including pharmacotherapy). Addiction is a complex bio-psycho-social 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 Medicine⁵⁴ guidance document.

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 dispensed in at OTP (in accordance with Federal law [42 CFR Part 8]), or prescribed by waived clinicians in any setting, including 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 Criteria⁵¹ for additional guidance).
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 (ie, 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 to 30 mg per day and the patient may be tapered off in approximately 6 to 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 (eg, 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.^{9–11}
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.
8. **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.

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 the dose 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 dispensing 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. While current federal regulations (42 CFR Part 8) include requirements for psychosocial treatment in OTPs, this can present barriers to access to treatment for some patients and is not consistent with the evidence base. 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 reinstated 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.
3. **Major Revision** Once objective signs of withdrawal are observed, initiation of buprenorphine should start with a dose of 2 to 4 mg. Dosages may be increased in increments of 2 to 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.^{13,14,36}
6. **New** The FDA recently approved several new buprenorphine formulations for treatment of opioid use disorder. 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 (eg, 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.
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*.⁸
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 to 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. **Minor Revision** Treatment with methadone or buprenorphine is recommended and should be initiated as early as possible during pregnancy.
2. **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.
3. **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.
4. 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.
5. **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.
6. 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.
7. **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 Medicine⁸ guidance document.
8. **Minor Revision** Care for pregnant women with opioid use disorder should be managed by a clinician experienced in obstetrical care and a clinician experienced in the treatment of opioid use disorder.
9. Hospitalization during initiation of methadone or buprenorphine may be advisable due to the potential for adverse events, especially in the third trimester.
10. **Major Revision** Methadone should be initiated at a dose range of 10 to 30 mg. Incremental doses of 5 to 10 mg is recommended every 3 to 6 hours, as needed, to treat withdrawal symptoms, to a maximum first day dose of 30 to 40 mg.
11. **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.
12. **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.

13. **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.
14. **Minor Revision** Use of naloxone challenge to test for opioid dependence and risk of precipitated withdrawal is not recommended for pregnant women with opioid use disorder.
15. **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 (eg, 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 (ie, 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 agonist 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 agonist 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 to 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 (eg, 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 (eg, 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 Criteria⁵).

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

1. **Minor Revision** All patients with opioid use disorder should receive a comprehensive assessment including determination of mental health status and suicide risk, including evaluation of whether the patient is stable. Patients with suicidal or homicidal ideation should be referred immediately for treatment and possibly hospitalization.
2. Management of patients at risk for suicide should include reducing immediate risk, managing underlying factors associated with suicidal intent, and monitoring and follow-up.
3. **Minor Revision** All patients with psychiatric disorders should be asked about suicidal ideation and behavior. Patients with a history of suicidal ideation or attempts should have adherence for opioid use disorder and psychiatric disorder medications monitored more closely.
4. **Minor Revision** Assessment for psychiatric disorder should occur at the onset of agonist or antagonist treatment. 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. Reassessment using a detailed mental status examination should occur after stabilization with methadone, buprenorphine, or naltrexone.
5. **Major Revision** Pharmacotherapy in conjunction with psychosocial treatment should be offered to patients with opioid use disorder and a co-occurring psychiatric disorder. 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.
6. Clinicians should be aware of potential interactions between medications used to treat co-occurring psychiatric conditions and opioid use disorder.
7. Assertive community treatment should be considered for patients with co-occurring schizophrenia and opioid use disorder who have a recent history of, or are at risk of, repeated hospitalization or homelessness.

Part 12: Special Populations: Individuals in the Criminal Justice System

1. **New** All FDA approved medications for the treatment of opioid use disorder should be available to individuals receiving healthcare within the criminal justice system. The treatment plan, including choice of medication, should be based on the patient's individual clinical needs.
2. **Minor Revision** Continuation of treatment after release results in a substantial reduction in all-cause and overdose mortality. Treatment should be individualized, and patients should receive complete information to make informed decisions in consultation with a medical and treatment team.
3. **New** Individuals entering the criminal justice system should not be subject to forced opioid withdrawal. Patients being treated for opioid use disorder at the time of entrance into the criminal justice system should continue their treatment. Patients with opioid use disorder who are not in treatment should be assessed and offered individualized pharmacotherapy and psychosocial treatment as appropriate.
4. **Major Revision** Initiation or maintenance of pharmacotherapy for the treatment of opioid use disorder is recommended for individuals within the criminal justice system (including both jails and prisons). Criminal justice staff should coordinate care and access to pharmacotherapy to avoid interruption in treatment. Patients should not be forced to transition from agonist (methadone or buprenorphine) to antagonist (naltrexone) treatment.
5. **Major Revision** Individuals in the criminal justice system who have opioid use disorder or who are experiencing opioid withdrawal should be offered a combination of pharmacotherapy and psychosocial treatment (based on an assessment of their individual psychosocial needs). 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.
6. **New** If an OTP is not accessible, providers may need to transition individuals from methadone to buprenorphine. Effectively transitioning from methadone to buprenorphine can be challenging but can be achieved safely if managed by a provider experienced in the procedure.

7. **Major Revision** Risk for relapse and overdose is particularly high in the weeks immediately following release from prison and jails. Patients being treated for opioid use disorder while in prison or jail should be stabilized on pharmacotherapy (methadone, buprenorphine or naltrexone) and continue in treatment after their release. Patient care on reentry to the community should be individualized and coordinated with treatment providers in the community.
8. **New** Naloxone kits should be available within correctional facilities. Individuals with opioid use disorder should receive a naloxone kit prior to release, and individuals and families should be educated in how to administer naloxone.

Part 13: Naloxone for the Treatment of Opioid Overdose

1. **Major Revision** Naloxone should be administered in the event of a suspected opioid overdose.
2. **Minor Revision** Naloxone may be administered to pregnant women in cases of overdose to save the mother's life.
3. **Minor Revision** Patients who are being treated for opioid use disorder (as well as people with a history of opioid use disorder leaving incarceration) and their family members/significant others should be given naloxone kits or prescriptions for naloxone. Patients and family members/significant others should be trained in the use of naloxone in overdose.
4. The Guideline Committee, based on consensus opinion, recommends that first responders such as emergency medical services personnel, police officers, and firefighters be trained in and authorized to carry and administer naloxone.

SUMMARY OF FINDINGS

Grounded in findings from a focused literature search, the RAM Process resulted in new recommendations to Part 1 (Assessment Recommendations), Part 2 (Treatment Options), Part 5 (Buprenorphine), Part 9 (Part 9: Special Populations: Individuals With Pain), and Part 12 (Special Populations: Individuals in the Criminal Justice System) of the Practice Guideline. At least one major or one minor revision was made in every part of the Practice Guideline.

Among the new and updated recommendation statements, the following represent significant shifts in recommended clinical practices from the 2015 publication. ASAM recommends that psychosocial treatment should be offered in conjunction with pharmacotherapy. However, a patient's decision to decline psychosocial treatment or the absence of available psychosocial treatment should not preclude or delay pharmacotherapy. Opioid withdrawal management with buprenorphine should not be initiated until there are objective signs of opioid withdrawal. The U.S. FDA recently approved several new buprenorphine formulations for treatment of opioid use disorder. As the data regarding the effectiveness of these products are currently limited, clinicians should use these products as labeled and be mindful of emerging evidence as it becomes available. Both office-based and home-based buprenorphine inductions are considered safe and

effective. Oral naltrexone is not recommended except under limited circumstances. Buprenorphine is a reasonable and recommended alternative to methadone for pregnant women. Naloxone should be administered for suspected overdose by those who have received overdose response education.

With respect to criminal justice settings. The focused update recommends several key changes to the previous clinical guidance. For example, all U.S. FDA approved medications for the treatment of opioid use disorder, should be available to patients within the criminal justice system, and the treatment plan, including choice of medication, should be based on the patient's individual clinical needs. Individuals entering the criminal justice system should not be subject to forced opioid withdrawal. Patients being treated for opioid use disorder at the time of entrance into the criminal justice system should continue their treatment. Patients with opioid use disorder not in treatment at the time of entrance into the criminal justice system should be assessed and offered individualized pharmacotherapy and psychosocial treatment as appropriate. Risk for relapse and overdose is particularly high in the weeks immediately following release from prison and jails. Patients being treated for opioid use disorder while in prison or jail should be stabilized on pharmacotherapy (eg, methadone, buprenorphine or naltrexone) and continued on treatment after their release. Patient care on reentry to the community should be individualized and coordinated with treatment providers in the community. Naloxone kits should be available within correctional facilities. Individuals with opioid use disorder, those with a history of opioid use disorder at risk for relapse, and potential bystanders should receive naloxone kits and training in how to administer naloxone.

CONCLUSION

Since 2015, important new developments (in the form of newly available formulations and medications), published evidence, and clinical guidance related to the treatment of addiction involving opioid use have emerged. As a result, ASAM has made several important updates and is publishing the Focused Update for the ASAM National Practice Guideline for Treatment of Opioid Use Disorder.

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