Regulatory Advisory Panel on Opioid Regulations

Virginia Board of Medicine

January 6, 2017

9:00 a.m.

Regulatory Advisory Panel on Opioid Regulations

Board of Medicine
Friday, January 6, 2017 @ 9:00 a.m.
9960 Mayland Drive, Suite 201 – Training Room 2
Henrico, Virginia

Call to Order

Emergency Egress Instructions i

Introductions

Charge of the Panel

Adoption of the Agenda

Public Comment on Agenda Items

New Business

1. Development of regulations for the use of buprenorphine in office-based treatment of addiction
   - Highlighted review of draft guidance document on the use of buprenorphine 1-32
   - Review of draft regulations 33-35
   - Discussion of DMAS regulations and ARTS information 36-40
   - Edits, additions, deletions to draft regulations ..... -------

2. Development of regulations for the use of opioid analgesics for pain and proper prescribing
   - Highlighted review of current Guidance Document 85-24 41-59
   - Review of draft regulations 60-62
   - Discussion of CDC guidelines 63-97
   - Edits, additions, deletions to draft regulations ..... -------

3. Recommendations to the Legislative Committee and Full Board

4. Next steps

Travel reminder .....

Adjournment

PERIMETER CENTER CONFERENCE CENTER
EMERGENCY EVACUATION OF BOARD AND TRAINING ROOMS
(Script to be read at the beginning of each meeting.)

PLEASE LISTEN TO THE FOLLOWING INSTRUCTIONS ABOUT EXITING THESE PREMISES IN THE EVENT OF AN EMERGENCY.

In the event of a fire or other emergency requiring the evacuation of the building, alarms will sound.

When the alarms sound, leave the room immediately. Follow any instructions given by Security staff

Training Room 2

Exit the room using one of the doors at the back of the room. **(Point)** Upon exiting the doors, turn **LEFT.** Follow the corridor to the emergency exit at the end of the hall.

Upon exiting the building, proceed straight ahead through the parking lot to the fence at the end of the lot. Wait there for further instructions.

Guidance Document 85-3

December 2, 2016

Guidance on Office-Based Treatment of Opioid Use Disorder

Prefacing Comment

The Governor's Task Force on Prescription Drug and Heroin Abuse, formed in September 2014, recommended in late 2015 that the Board of Medicine form a work group to review the literature on buprenorphine and to make recommendations on acceptable practices for the Board's consideration of promulgating regulations. The Board assembled its Work Group on Buprenorphine in early 2016. The effort brought together physicians of various specialties that were experienced in the treatent of opioid use disorder with buprenorphine as well as representatives from state governmental agencies and insurance companies. At its first meeting on May 13, 2016, the Work Group chose to use the Federation of State Medical Boards "Model Policy on DATA 2000 and Treatment of Opioid Addiction in the Medical Office" (2013) as its starting point. With the permission of the Federation, the Model Policy has been edited and revised by the Work Group as its representation of acceptable practices for the physicians, physician assistants, nurse practitioners, and citizens of the Commonwealth. All references in the FSMB document remain included at the end.

Work Group Members

David Buchsbaum, MD
Martin Buxton, MD
Lawrence Conell, MD
Margaret Gregorczyk, MD
Caroline Juran, RPh
Matthew Keats, MD
Robert Lowe, MD
Mary McMasters, MD
Mark Mattingly, MD
Renee Miskimmin, MD
Katherine Neuhausen, MD
Ralph Orr
Donna Proffitt
Mellie Randall
James Reinhard, MD
Mark Stevens, MD
Kenneth Walker, MD, Chair
William L. Harp, MD

With assistance from Hughes Melton, MD and Art Van Zee, MD

Introduction

The profile of opioid addiction in the United States is changing, in that nonmedical use of prescription opioids has become a problem as significant as the use of heroin. Recent data indicate that approximately 1.6 million persons in the U.S. misused or were addicted to prescription opioids in 2010 [1], while 323,000 persons misused or were addicted to heroin [2]. Despite the dimensions of the problem, nearly 80% of opioid-addicted persons do not receive treatment for their addiction because of limited treatment capacity, financial obstacles, social stigma, and other barriers to care [3].

To address this need, researchers, federal health agencies, and pharmaceutical manufacturers have focused on developing medications that can be used to treat opioid addiction in medical office settings, rather than being limited to use only in specialized Opioid Treatment Programs (OTPs) [4]. As a result of those efforts, two major products are now available for use in office settings: buprenorphine (alone and in combination with naloxone) and naltrexone (in an oral formulation and an extended-release injectable formulation). These medications have been shown to be effective when used in office-based settings in conjunction with behavioral health services, and it is the Board's desire to increase access to medication-

assisted treatment (MAT) for patients with addiction in office-based settings as well as other qualified practice settings.

Regardless of setting, the primary goals of addiction treatment are to cease opioid misuse and abuse and to improve the patient's overall health and social functioning, and to help the patient avoid some of the more serious consequences of opioid use disorder. Treatment can also help patients see their problems from a different perspective, improve self-reliance, and empower them to make positive changes in their lives [8].

Buprenorphine: Buprenorphine is a partial opioid agonist that was approved by the FDA to treat opioid addiction in 2002. It is available in multiple formulations, both as a mono-product of buprenorphine and combined with naloxone. The addition of naloxone to buprenorphine does not reduce the efficacy of the medication when it is taken sublingually, yet it appears to serve as a deterrent to injection misuse [9]. For this reason, the buprenorphine/naloxone combination is the preferred formulation for nearly all patients, with the possible exception of pregnant women, for whom current guidelines recommend use of the mono-product [10]. Physicians should use their clinical judgement to determine if there is a compelling medical reason to use mono-products for non-pregnant patients. Exceptions should be rare, bearing in mind that the presenting history may be inaccurate. Whenever the mono-product is used, extra attention should be given to the risks of misuse and diversion.

Multiple studies have shown that, administered sublingually and at therapeutic doses in appropriately selected patients, buprenorphine is safe and effective [11-15]. The blockade of the opioid receptor imposed by buprenorphine limits the effects of subsequently administered opioid agonists or antagonists, reducing the risk of opioid overdose. The "ceiling effect" appears to confer a higher safety profile and generally milder withdrawal symptoms (compared to full agonists) when the drug is tapered after prolonged administration [16-17].

Nevertheless, overdoses and deaths due to buprenorphine can occur and have been reported [18]. Most overdoses, especially fatal ones, involve concurrent use of other CNS depressants, such as benzodiazepines, other opioids, or alcohol [19-22]. Buprenorphine also poses a significant risk to non-tolerant individuals, especially children [23].

Relatively few serious adverse events have been associated with buprenorphine. Where such events have been reported, most have involved abuse of the drug by injection, rather than sublingual administration in a clinical setting [24-28]. A national evaluation of pharmacotherapies for opioid addiction in Australia involving more than 1,200 patients found no significant difference in rates of serious adverse events between methadone, LAAM, and buprenorphine, or between different doses of buprenorphine [29].

Although early reports based on animal studies suggested that buprenorphine would have a low potential for misuse to achieve euphoria, researchers have documented a measurable level of misuse and diversion of buprenorphine [30-31]. Varying levels of misuse and diversion were predicted by early investigators [32] because buprenorphine is prescribed to high-risk individuals who are addicted to opioids. Subsequent research confirms that misuse and diversion have been reported worldwide wherever buprenorphine has been used for the treatment of addiction [33-36].

Role of Federal Legislation: The use of buprenorphine for the treatment of opioid addiction is governed by the federal Drug Addiction Treatment Act of 2000, commonly referred to as "DATA 2000" (Public Law 106-310, Title XXXV, Sections 3501 and 3502). This legislation is of particular interest to state medical boards because, for the first time in almost a century, it allows physicians to treat opioid addiction with FDA-approved controlled drugs in office-based settings. Specifically,

DATA 2000 allows physicians to use buprenorphine and other controlled substances in CSA Schedules III, IV, and V, which have been approved by the FDA for the treatment of opioid dependence, to treat patients in office-based settings, provided certain conditions are met.

DATA 2000 thus has enlarged treatment capacity by lifting the requirement that patients who need opioid agonist treatment can receive such treatment only in specially licensed opioid treatment programs (OTPs), often referred to as "methadone clinics."

Implementation of DATA 2000 required changes in the oversight systems within the Department of Health and Human Services (HHS) and the Drug Enforcement Administration (DEA). The Secretary of HHS delegated authority in this area to the Center for Substance Abuse Treatment (CSAT) of the Substance Abuse and Mental Health Services Administration (SAMHSA).

Role of State Medical Boards: The use of opioid agonist medications to treat opioid-addicted patients in the offices of individual physicians significantly increases the role of state medical boards in overseeing such treatment. For this reason, the Federation of State Medical Boards entered into an agreement with SAMHSA to develop model guidelines for use by state medical boards in regulating office-based treatment of addiction. This resulted in the Model Policy adopted by the Federation in 2002 [37].

The Model Policy presented here reflects the large body of research and experience accrued in the decade since buprenorphine was approved in 2002 for the treatment of opioid addiction. The Model Policy is designed to encourage state medical boards to adopt consistent standards, to promote the public health by making appropriate treatment available to opioid-addicted patients, and to educate the regulatory and physician communities about the potential of new treatment modalities for opioid addiction.

The Federation acknowledges with gratitude the efforts of the state Board members and directors who worked to update the Model Policy, as well as the contributions of the independent experts and medical organizations that advised the drafting committee and reviewed its work. The Federation also thanks SAMHSA for its support of this important project.

Section I: Preamble

The Virginia Board of Medicine is obligated under the laws of the Commonwealth of Virginia to protect health and safety of the public through regulation of healthcare professionals. The Board recognizes that enforcing the principles of sound medical practice will ensure that the people of Virginia have access to appropriate, safe and effective medical care, including the treatment of addiction. The application of up-to-date knowledge and evidence-based treatment modalities can help to restore function and thus improve the quality of life of patients who suffer from addiction. Accordingly, the Board acknowledges the body of evidence for the effectiveness of buprenorphine in the office-based treatment of opioid addiction [38], when such treatment is delivered in accordance with current standards of care and the requirements of the Drug Addiction and Treatment Act of 2000 (DATA 2000).

Federal Requirements to Prescribe Buprenorphine for Addiction: Physicians who wish to treat opioid addiction with buprenorphine in their medical offices must demonstrate that they have met the requirements of the DATA 2000 legislation and obtained a waiver from SAMHSA.[i] To qualify for such a waiver, physicians must hold a current controlled substance registration with the Drug Enforcement Administration and a current license in the state in which they practice. They also must meet one or more of the following qualifications [39]:

- Subspecialty board certification in addiction psychiatry from the American Board of Medical Specialties
- Subspecialty board certification in addiction medicine from the American Osteopathic Association
- Addiction certification from the American Board of Addiction Medicine
- Completion of not less than eight hours of training related to the treatment and management of opioid addiction provided by the American Academy of Addiction Psychiatry, the American Society of Addiction Medicine, the American Medical Association, the American Osteopathic Association, the American Psychiatric Association, or other approved organizations
- Participation as an investigator in one or more clinical trials leading to the approval of an opioid drug in Schedule III, IV, or V or a combination of such drugs for treatment of opioid-addicted patients

To obtain a waiver, a physician must notify SAMHSA in writing of his/her intent to prescribe an approved opioid medication to treat addiction, certifying the physician's qualifications and listing his/her DEA registration number. SAMHSA will then notify DEA whether a waiver has been granted. If SAMHSA grants a waiver, DEA will issue an identification number no later than 45 days after receipt of the physician's written notification. If SAMHSA does not act on the physician's request for a waiver within the 45-day period, DEA will automatically assign the physician an identification number. This process is explained, and can be accessed at the following website: http://buprenorphine.samhsa.gov/howto.html.

If a physician wishes to prescribe or dispense an appropriately available and approved opioid medication for maintenance treatment or detoxification on an emergency basis before the 45-day waiting period has elapsed, the physician must notify SAMHSA and the DEA of his/her intent to provide such emergency treatment.

In addition to a waiver, a physician who wishes to prescribe buprenorphine or another approved opioid for the treatment of addiction in the office setting must have a valid DEA registration number and a DEA identification number that specifically authorizes him or her to engage in office-based opioid treatment.

Prescription Requirements: Prescriptions for buprenorphine and buprenorphine/naloxone must include full identifying information for the patient, including his/her name and address, the drug name, strength, dosage form, quantity, and directions for use. Prescriptions for buprenorphine and/or buprenorphine/naloxone must be dated as of, and signed on, the day they are issued. (21)

---

[i] The "waiver" allows an exception to the Harrison Narcotics Act of 1914, which made it illegal for a physician to prescribe an opioid to any patient with opioid addiction for the purpose of managing that addiction or acute withdrawal. Prior to DATA 2000, the only exception to the Harrison Act was federal legislation that allowed the establishment of methadone maintenance treatment (MMT) clinics, now referred to as Opioid Treatment Programs (OTPs). That exception only allowed the use of methadone to treat addiction or withdrawal within specially licensed and regulated facilities, but not in office-based medical practices (CFR 1306.05[a]). Both the physician's regular DEA registration number and the physician's DATA 2000 identification number (which begins with the prefix X) must be included on the prescription (21 CFR 1301.28 [d][3]). [39]

For detailed guidance, physicians are referred to the Buprenorphine Clinical Practice Guidelines published by CSAT/SAMHSA, which can be accessed at http://www.samhsa.gov/centers/ csat/opat.html.

State Medical Board Requirements: The Virginia Board of Medicine will determine the appropriateness of a particular physician's prescribing practices on the basis of that physician's overall treatment of patients and the available documentation of treatment plans and outcomes. The goal is to provide appropriate treatment of the patient's opioid addiction, either directly or through referral, while adequately addressing other aspects of the patient's functioning, including co-occurring medical and psychiatric conditions and pressing psychosocial issues.

Section II: Guidelines

Multiple studies have shown that opioid addiction treatment with buprenorphine can be successfully integrated into office practice by physicians who are not addiction specialists. In such studies, patient outcomes are comparable to or better than outcomes of patients treated in specialized clinics [40-48]. However, as in the treatment of any medical disorder, physicians who choose to offer addiction treatment need to understand the nature of the underlying disorder, the specific actions of each of the available medications, as well as any associated contraindications or cautions, and the importance of careful patient selection and monitoring [40].

The Board has adopted the following guidelines for the treatment of opioid addiction in office-based settings. The guidelines are not a complete compendium on best practices in qualified office practice settings, but rather a communication to prescribers regarding what the Board considers to be acceptable professional practice.

Physician Qualifications: The diagnosis and medical management of the disease of addiction, including opioid addiction, should be based on current knowledge and research and should encompass the use of both pharmacologic and nonpharmacologic treatment modalities. Thus, before beginning to treat patients for opioid addiction, the physician should become knowledgeable about opioid addiction and its treatment, including the use of approved pharmacologic therapies and evidence-based nonpharmacologic therapies [49-50].

As described in the Preamble, physicians who wish to prescribe or dispense buprenorphine for the treatment of opioid addiction must meet the requirements of DATA 2000 [51], which are that the physician must be licensed in the state, have a valid DEA controlled substances registration and identification number, comply with federal and state regulations applicable to controlled substances, and hold a current waiver [39].

In addition to these requirements, regulations limit the number of patients that a physician is permitted to treat at any one time to 30 in the first year after obtaining a waiver, then 100 for a year or more, and then to 275 patients thereafter. The physician who wishes to treat more than 30 patients after the first year must file an application with the DEA to extend his/her waivered capacity to do so [39,51]. Likewise, a physician who has treated 100 patients for at least one year must apply to treat up to 275 patients per year. To do so, a physician must have additional credentialing or practice in a qualified practice setting. Details can be found at http://www.samhsa.gov/sites/default/files/programs_campaigns/medication_assisted/understanding-patient-limit275.pdf

DATA 2000 also requires that a physician who wishes to treat opioid addiction with buprenorphine in the office setting must demonstrate a capacity to offer, or refer patients for, appropriate counseling and other ancillary services, and to recognize when those services are needed [51].

Physicians have not been permitted to delegate the prescribing of buprenorphine to non-physicians. However, with the passage of the Comprehensive Addiction and Recovery Act in July 2016, physician assistants and nurse practitioners will be able to prescribe buprenorphine for opioid use disorder.

Physician assistants and nurse practitioners must take 24 hours of training on the topics of opioid maintenance and detoxification, clinical use of all FDA-approved drugs for medication-assisted treatment, patient assessment, treatment planning, psychosocial services, staff roles and diversion control. They will be able to apply in early 2017 to treat 30 patients.

Physicians should review and comply with the DEA regulations (Title 21 US Code of Controlled Substances Act 1301.28 and 21 USC 823 9GO(2)(G) [51]. Review of the resources available on the DEA's website (at www.deadiversion.usdoj.gov) , the Virginia Drug Control Act, Board of Pharmacy and Board of Medicine regulations and guidance documents governing the issuance of prescriptions for controlled substances is strongly recommended.

Patient Assessment: The following is not meant to be an all-inclusive list but suggestive of what needs to be in the assessment. For more details, refer to the American Society of Addiction Medicine National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Abuse.

The objectives of the patient assessment are to determine a given patient's eligibility for treatment, to provide the basis for a treatment plan, and to establish a baseline measure for use in evaluating a patient's response to treatment. Accordingly, the assessment should be designed to achieve the following [49,53]:

- Establish the diagnosis of opiate addiction, including the duration, pattern and severity of opioid misuse; the patient's level of tolerance; results of previous attempts to discontinue opioid use disorder; past experience with agonist therapies; the nature and severity of previous episodes of withdrawal; and the time of last opioid use and current withdrawal status
- Document the patient's use of other substances, including alcohol and other drugs of abuse, date of last use, route of administration, injection history, intranasal use, presence of track marks, and history of seizures
- Identify comorbid medical and psychiatric conditions and disorders and to determine how, when and where they will be addressed
- Screen for communicable diseases and address them as needed
- Evaluate the patient's level of physical, psychological and social functioning or impairment
- Assess the patient's access to social supports, family, friends, employment, housing, finances and legal problems
- Determine the patient's readiness to participate in treatment

Assessment usually begins at the time of the patient's first office visit and continues throughout treatment. Consensus opinion is that an initial patient assessment should include the following:

- Medical and psychiatric history
- Substance abuse history
- Evaluation of family and psychosocial supports
- Appropriate examination in accordance with state and federal law, COV §54.1-3303, focused on evaluating neurocognitive function, identifying sequelae of opioid addiction, and looking for evidence of severe hepatic dysfunction [10,53]
- Urine drug screen or other toxicologic screen should be included in the initial evaluation to confirm recent opioid use disorder and to screen for unreported use of other drugs
- Access the patient's prescription drug use history through the Virginia Prescription Monitoring Program, both to confirm compliance in taking prescribed medications and to detect any unreported use of other prescription medications

The drug screen should include all opioids commonly prescribed and/or misused in the local community, as well as illicit drugs that are available locally [54]. It also is advisable to strongly suggest a pregnancy test for all women of childbearing age and HIV, Hepatitis B and C, and tuberculosis testing for all patients.

Information from family members and significant others can provide useful additional perspectives on the patient's status, as can contact with or records from clinicians who have treated the patient in the past [46].

Treatment Planning: There is an emerging consensus among addiction experts that treatment medications such as buprenorphine should be considered as an option for every opioid-addicted patient [38]. However, the failure to offer medication-assisted treatment does not in itself constitute substandard care. No single treatment is appropriate for all persons at all times. Therefore, an individualized treatment plan is critical to the patient's ultimate success in returning to productive functioning [5,54].

The treating physician should balance the risks and benefits of medication-assisted treatment in general, and treatment with buprenorphine in particular, against the risks associated with no treatment or treatment without medication [4,55]. Psychosocial and other nonpharmacologic interventions often are useful components of treatment [48,50,55]. Such interventions typically work best in conjunction with medication-assisted therapies. In fact, there is some evidence that the combination of pharmacologic and non-pharmacologic interventions may be more effective than either approach used alone [56]. As noted earlier, the ability to offer patients psychosocial supports, either on-site or through referral, is a requirement of the DATA 2000 legislation. Given that the evidence for the combination of buprenorphine products and psychosocial supports results in better outcomes for patients, this combined treatment approach is considered best practice unless there are specific reasons not to use it. In cases where combined treatment is not appropriate for a particular patient other options may include:

- Simple detoxification under limited circumstances and no other treatment
- Detoxification followed by antagonist therapy
- Counseling and/or peer support without medication-assisted therapy
- Referral to short- or long-term residential treatment
- Referral to an OTP for methadone maintenance

Patients may be suitable candidates for treatment with buprenorphine even if past treatment episodes were not successful [50].

If a decision is made to offer the patient treatment with buprenorphine, the risks associated with possible misuse and diversion are such that the combination buprenorphine/naloxone product is preferable for most patients [38,40,43]. Since the mono-product does have higher diversion and abuse potential, it should be rarely used, excepting pregnancy and breastfeeding, and the reasons for choosing the mono-product should be well-documented in the medical record.

Educating the Patient: Every patient to whom buprenorphine is prescribed should be cautioned to follow the directions exactly, particularly during the induction stage. Critical points of education are when to begin dosing, the frequency of subsequent doses, and the importance of avoiding the use of any other illicit or prescription opioid. Concurrent use of non-opioid sedating medications or over-the-counter products should also be discussed. Patients should be advised to avoid the use of alcohol [7].

Patients should be cautioned about potential sedation or impairment of psychomotor function during the titration phase of induction with buprenorphine [57].

Finally, because opioids can contribute to fatal overdoses in individuals who have lost their tolerance to opioids or in those who are opioid-naïve, including children or other family members, proper and secure storage of the medication must be discussed. Particularly where there are young people in the patient's home, the subject of safe storage and use should be revisited periodically throughout the course of treatment, with the discussions documented in the patient record [57]. Prescribers should consider providing a naloxone prescription for emergency overdose situations.

Informed Consent: Although agonist medications such as buprenorphine are clearly effective for the treatment of opioid dependence, they do entail substitute physical dependence on the prescribed medication to replace the prior physical dependence on the misused opioid [46]. This issue should be thoroughly discussed with the patient in terms of potential risks and benefits as part of the informed consent process. Patients and family members often are ambivalent about agonist treatment for this reason, and their concerns may influence subsequent treatment choices. Possible topics of discussion include the difference between addiction and physical dependence, including an explanation of why agonist therapy is not simply "switching one addiction for another", the likelihood of relapse with and without medication-assisted treatment, the projected duration of treatment, the potential for successfully tapering from agonist therapy at some point in the future, and the role and importance of adjunctive therapies such as counseling and peer support. Other topics important to discuss might be the greatly reduced risk of overdose and death with buprenorphine as compared to illicit opioids, and that patients are more likely to be able to achieve their highest level of functioning with buprenorphine than with street drugs, which nearly always cause continued decline in functioning including incarceration, job loss, inability to parent children, etc. With the patient's consent, this conversation could include family members, significant other(s), or a guardian [7].

A written *informed consent* document, discussed with and signed by the patient, can be helpful in reinforcing this information and establishing a set of "ground rules." The practitioner should document the informed consent in the patient's medical record [58].

Treatment Agreement: The terms of *treatment agreements* vary widely, but typical provisions include an acknowledgement of the potential benefits and risks of therapy and the goals of treatment; identification of one provider and one pharmacy from whom the patient will obtain prescriptions; authorization to communicate with all providers of care (and sometimes significant others); to consult the Virginia Prescription Monitoring Program; other treatments or consultations in which the patient is expected to participate, including recovery activities; avoidance of illicit substances; permission for drug screens of blood, urine, saliva or hair/nails; pill counts as appropriate; mechanisms for prescription renewals, including exclusion of early renewals; expected interval between office visits; and specification of the conditions under which therapy will be continued or discontinued [59].

The agreement also should include a statement instructing the patient to stop taking all other opioid medications. Such a statement reinforces the need to adhere to a single treatment regimen. Inclusion in the agreement of a pharmacy address and telephone number reinforces to the patient the importance of using one pharmacy to fill prescriptions, with recognition that there may be exceptions to this for certain patients.

Finally, the treatment agreement should set forth the objectives that will be used to evaluate treatment success, such as freedom from intoxication, improved physical and psychosocial function, and adherence to the treatment regimen [59].

Copies of the treatment agreement and informed consent should be provided to the patient and all other care providers, and filed in the patient's medical record. The agreement should be reviewed regularly and revised as needed [58].

Induction, Stabilization, and Follow-up: The goal of induction and stabilization is to find the lowest dose of buprenorphine at which the patient discontinues the use of illicit opioids without experiencing withdrawal symptoms, significant side effects, or uncontrollable cravings for the drug of abuse [60].

In general, patients should not concurrently take buprenorphine products with benzodiazepines, sedative hyponotics, carisoprodol, or other opioids including tramadol due to the higher risk for fatal overdose. Stimulants are a separate area of concern given the theoretical risk of continuing to stimulate the dopamine reward pathways, theoretically increasing the risk of relapse. However, there may be patients in whom it is judged that the potential benefits of treating severe ADHD may outweigh the risks, in part via improved function and decreased impulsivity. There is data that untreated ADHD predisposes to substance use disorders and cautious treatment with careful monitoring may support substance use treatment and abstinence from other drugs of abuse. Clinical judgment and careful documentation are required in such cases, rather than hard and fast rules.

Practitioners should remain aware that it is now Virginia law that if he/she anticipates giving more than 14 days of an opioid, there must be a check of the Virginia Prescription Monitoring Program when initiating treatment.

The initial induction process requires a higher degree of attention and monitoring than the later maintenance phase [59]. Patients need to be seen more frequently during the induction or early treatment, typically 1-3 times per week. Particular attention should be given to the timing of the initial doses so as to minimize untoward outcomes. Withdrawal symptoms can occur if either too much or too little buprenorphine is administered. Spontaneous withdrawal can occur if too little buprenorphine is given. Precipitated withdrawal can occur if buprenorphine is administered while the opioid receptors are substantially occupied by an opioid agonist. Overmedication should be avoided by starting the patient on lower doses, such as 4 mg per day.

The stabilization phase is focused on finding the right dose for an individual patient. A patient is stabilized when the dose allows him/her to conduct activities of daily living and to be aware of his/her surroundings without intoxication and without suffering withdrawal or significant drug craving [61-62]. Although there is no precise way to determine in advance what the optimal dose for a particular patient will be [63], most patients will stabilize on 8 to 12 mg of buprenorphine per day. Rarely, some patients may need doses up to 24 mg per day [64].

Buprenorphine blood concentrations stabilize after approximately seven days of consistent dosing [17]. If withdrawal symptoms subsequently emerge during any 24-hour dosing interval, the dose may be too low. The patient should be assessed for other factors that can cause cravings and withdrawal prior to increasing the dose of buprenorphine. Medical factors that may cause a patient's dose requirements to change include, but are not limited to, starting, stopping, or changing the dose of other prescription medications; onset and progression of pregnancy; onset of menopause; progression of liver disease; and significant increase or decrease in weight [61].

Dose adjustments generally should be made in increments of 2 mg/day. Because buprenorphine has a long plasma half-life and an even longer duration of action at the mu opioid receptor, five to seven days should be allowed between dose adjustments [53].

Patient adherence to medication regimens and session appointments is associated with better treatment outcomes. Regular monitoring can help patients plan for possible obstacles and teach them ways to handle any problems that occur [65]. Regular assessment of the patient's level of engagement in treatment and the strength of the therapeutic alliance allows for modification of the treatment plan and level of care in response to the patient's progress or lack thereof [56].

Early in treatment, medications should be prescribed and follow-up visits scheduled commensurate with the patient's demonstrated stability. Until patients have shown the ability to be compliant with the treatment plan and responsible with their medication supplies, and have discontinued high-risk behaviors and associated diversion risks, they should be seen more frequently and given medication only needed until the next visit.

Clinicians should take steps to reduce the chances of buprenorphine diversion. Recommended strategies include using the lowest effective dose, frequent office visits, urine drug testing, including testing for buprenorphine and its metabolites, recall visits for medication dose counts, and checking the Virginia Prescription Monitoring Program.

As patients demonstrate stability and the risks decline, they can be seen less often, but at least monthly. Larger amounts of medication may be prescribed to last from visit to visit, but not to increase the dose [46,59].

It is strongly recommended that prescribers ensure that they are capable of providing psychosocial services, either in their own practices or through referrals to reputable behavioral health practitioners in the community. It is the prescriber's responsibility to ensure the patient receives psychosocial treatment. Failure of the patient to keep their psychosocial appointments should be considered non-compliance with the treatment plan.

Patient monitoring during follow-up visits should address the following points [46,54,59,66]:

- Whether the patient continues to use alcohol or illicit drugs, or to engage in non-medical use of prescription drugs
- The degree of compliance with the treatment regimen, including the use of prescribed medications as directed
- Changes, positive or negative, in social functioning and relationships
- Avoidance of high-risk individuals, situations, and diversion risks
- Review of whether and to what degree the patient is involved in counseling and other psychosocial therapies, as well as in self-help activities through participation in mutual support meetings of groups such as Narcotics Anonymous
- The presence or absence of medication side effects
- The presence or absence of medical sequelae of substance use and its remission
- Periodic urine drug screens, a minimum of four per year and more frequently based on clinical need
- Regular checks of the Prescription Monitoring Program, typically once a month and in accordance with the treatment plan

Individuals engaged in medication-assisted treatment often demonstrate dramatic improvement in addiction-related behaviors and psychosocial functioning. Such positive changes should be acknowledged and reinforced by the prescribing physician whenever possible. Reducing the frequency of monitoring visits, with their associated costs, and increasing the patient's responsibility for medications are examples of how positive, responsible behaviors can be reinforced [46,67].

Adjusting the Treatment Plan: Outcomes typically are positive for patients who remain in medication-assisted treatment such as with buprenorphine [46,68]. However, some patients struggle to discontinue their misuse of opioids or other drugs, are inconsistent in their compliance with treatment agreements, or succeed in achieving some therapeutic goals while not doing well with others [69].

Behaviors that are not consistent with the treatment agreement should be taken seriously and used as an opportunity to further assess the patient and adapt the treatment plan as needed. In some cases, where the patient's behavior raises concerns about safety or diversion of controlled medications, there may be a need to refer the patient for treatment in a more structured environment, such as an OTP, intensive outpatient program or residential treatment. [69]. With the exception of diversion, behavior that violates the treatment agreement or a relapse to nonmedical drug use may not automatically constitute grounds for termination of treatment. Rather, they should be taken as a signal to reassess the patient's status, to implement changes in the treatment plan as by intensifying the treatment structure or intensity of services, and to document such changes in the patient's medical record [46].

Whenever the best clinical course is not clear, consultation with another practitioner may be helpful. The results of the consultation should be discussed with the patient and any written consultation reports added to the patient's record [59].

Patients with more serious or persistent problems may benefit from referral to a specialist for additional evaluation and treatment. For example, the treatment of addiction in a patient with a comorbid psychiatric disorder may be best managed through consultation with or referral to a specialist in psychiatry or addiction psychiatry [10]. In other instances, aberrant or dysfunctional behaviors may indicate the need for more vigorous engagement in peer support, counseling, or psychotherapies, or possibly referral to a more structured treatment setting [56].

Preventing and Managing Relapse: Relapse should always be ruled out as a reason for loss of stability [56]. Relapse to drug use has been described as "an unfolding process in which the resumption of substance abuse is the last event in a long series of maladaptive responses to internal or external stressors or stimuli" [70]. It rarely is caused by any single factor; rather, it is a dynamic process in which the patient's readiness to change interacts with other external and internal factors [59, 71]. Patients in relapse vary in the quantity and frequency of their substance use, as well as the accompanying medical and psychosocial sequelae.

Clinical strategies to prevent and address relapse generally encompass the following steps [10,61,71]:

- Identify environmental cues and stressors that act as relapse triggers
- Help patients develop skills to cope with or manage negative emotional states
- Help the patient work toward a more balanced lifestyle
- Understand and manage craving
- Identify and interrupt lapses and relapses. Patients should have an emergency plan to address a lapse so that a full-blown relapse can be avoided. If relapse does occur, be prepared to intervene
- Develop a recovery support system. Families are more likely to provide such support if they are engaged in the treatment process and have an opportunity to ask questions, share their concerns and experiences, and learn practical coping strategies and behaviors to avoid
- Consult with psychiatry in the circumstance of multiple relapses

It should be noted that lack of adherence to pharmacologic regimens occurs in a substantial portion of patients being treated for addiction, with some studies reporting that a majority of patients fail to follow

the treatment plan at some point in their care. Retention in treatment also is a problem [72]. This is no different from the challenges encountered in managing any chronic disease, such as diabetes, hypertension, epilepsy, and other potentially life-threatening disorders [46], and is not an indication to terminate treatment.

Patients who continue to misuse opioids after sufficient exposure to buprenorphine and psychosocial services or who experience continued symptoms of withdrawal or craving at 16 mg of buprenorphine should be considered for therapy with methadone [5,7,52,73].

Duration of Treatment: Available evidence does not support routinely discontinuing medication-assisted treatment once it has been initiated and the patient has stabilized. However, this possibility frequently is raised by patients or family members. When it is, the physician and patient should carefully weigh the potential benefits and risks of continuing medication-assisted treatment and determine whether buprenorphine therapy can be safely discontinued [74].

Studies indicate that opioid-dependent patients are at high risk for relapse when medication-assisted therapy is discontinued, even after long periods of stable maintenance [7,74]. Research also shows that longer duration of treatment is associated with better treatment outcomes. Such long-term treatment, which is common to many medical conditions, should not be seen as treatment failure, but rather as a cost-effective way of prolonging life and improving the quality of life by supporting the natural and long-term process of change and recovery. Therefore, the decision to discontinue treatment should be made only after serious consideration of the potential consequences [3,7-8].

As with any other disease, the continuation of medication-assisted treatment should be linked directly to the patient's response, for example, his/her attainment of treatment goals. Relapse risk is highest in the first 6 to 12 months after initiating abstinence, and the risk gradually diminishes over a period of years. Therefore, it is reasonable to continue treatment for at least a year if the patient responds well, [3,7,10]. However, some patients may require longer treatment with buprenorphine products.

If buprenorphine is discontinued, the patient should be tapered off the medication through use of a safely structured regimen, and followed closely [46]. It may be necessary to reinstate pharmacotherapy with buprenorphine or a different medication or other treatment services if relapse appears imminent or actually occurs [59]. Such relapse poses a significant risk of overdose, which should be carefully explained to the patient [74]. Patients also should be assured that relapse need not occur for them to be reinstated to medication-assisted therapy [46].

Medical Records: Accurate and up-to-date medical records protect both the physician and the patient. In the event of a legal challenge, detailed medical records that document what was done and why are essential elements of the practitioner's defense [75-76].

A written informed consent and a treatment agreement articulating measurable treatment goals are key documents. The treatment agreement should be updated as new information becomes available. Both the informed consent and treatment agreement should be carefully explained to the patient and signed by both the patient, guardian if applicable, and the treating physician [76]. The document should reflect that the patient may be required to participate in observed urine drug screens, call backs for medication counts, and checks of the Prescription Monitoring Program. The medical record should clearly reflect the decision-making process that resulted in any given treatment regimen.

The patient's chart should contain a summary of the information needed to understand the treatment plan, even without a thorough knowledge of the patient. This includes some demographic data, the names of other practitioners caring for the patient, all diagnoses, therapies employed, and a list of all medications

prescribed. The name, telephone number, and address of the patient's pharmacy also should be recorded to facilitate contact as needed [10,76].

Other documents that should be part of the medical record, where available, include [10,74,76]:

- Diagnostic assessments, including the patient history, physical examination, and any laboratory tests ordered, with their results
- Actual copies of, or references to, medical records of past hospitalizations or treatments by other providers
- The treatment plan, treatment agreement, and informed consent
- Authorization for release of information to other treatment providers
- Documentation of discussions with and consultation reports from other health care providers
- Medications prescribed and the patient's response to them, including any adverse events

The medical record must also include all prescription orders, whether written or telephoned. In addition, written instructions for the use of all medications should be given to the patient and documented in the record [75].

Monitoring visits should be carefully documented in the medical record, along with any subsequent changes to the treatment plan [10,76]. The patient's record should also contain documentation of steps taken to prevent the diversion of treatment medications, including any communications with other treating physicians and use of the Prescription Monitoring Program to verify that all prescribed medicines have been obtained and that no other prescriptions for controlled drugs have been dispensed without the physician's knowledge [77-78].

Records, including drug logs if buprenorphine is dispensed in the office, should be up-to-date and maintained in an accessible manner, readily available for review [75]. Good records demonstrate that a service was provided to the patient and establish that the service provided was medically necessary. Even if the outcome is less than optimal, thorough records can protect the physician as well as the patient [10,74,76].

Physicians who treat patients for addiction must observe the special confidentiality requirements of federal law 42 CFR, Part 2, which addresses the confidentiality of patients being treated for alcohol or drug addiction. 42 CFR Part 2 prohibits release of records, redisclosure, or other information without the patient's consent or a valid court order, or in cases of a *bona fide* medical emergency, or in the course of mandatory reporting of child abuse [7].

Section III: Special Populations

The Work Group members with expertise in treating certain groups of patients were asked to provide guidance for their colleagues engaged in buprenorphine treatment of substance use disorders. Names of the members follow the sections.

Treatment of Pregnant Women with Buprenorphine

- Opioid use disorder among pregnant women is increasingly common, and the cost to society, especially in terms of treating premature babies and/or those with neonatal abstinence syndrome, is staggering.

- As with all patients with opioid use disorder, pregnant women achieve abstinence from illicit opioid and other drug use roughly ten times more often with medication-assisted treatment than with abstinence-based treatment.

- Treatment of pregnant women with opioid use disorder with buprenorphine reduces risk of prematurity and greatly reduces the incidence of neonatal abstinence syndrome.

- Therefore, all pregnant women that present already addicted to opioids should be encouraged to accept medication-assisted treatment.

- Methadone is still acceptable, but buprenorphine is preferable for most women not already on methadone. There is less overdose risk with buprenorphine, and fetal outcomes are better.

- Buprenorphine mono-product is still the recommended form of buprenorphine for pregnant and breastfeeding women, but growing evidence suggests that use of the buprenorphine-naloxone combination is equivalent in efficacy and safety, and may be more appropriate for some patients, especially those at high risk for IV misuse of the buprenorphine mono-product.

- Pregnant women should be counseled to take buprenorphine only as prescribed, and reasonable steps should be taken to discourage diversion and misuse of buprenorphine. Such steps might include increased frequency of visits, examination for evidence of nasal and IV use, and periodic random call-backs for drug screens and pill counts.

- In addition to seeing pregnant women on buprenorphine more frequently, the physician should give special attention to ensuring psychosocial supports to help improve compliance with treatment. This may include seeing the substance abuse counselor and/or recovery coach more frequently, supportive counseling with the physician, and/or group therapy and peer support groups.

- Most pregnant women will not require more than 16mg of buprenorphine daily, and many can be managed with 8mg or less.

- Acute opioid withdrawal causes fetal distress and can cause fetal demise, and needs to be avoided throughout treatment. Despite this, a pregnant woman unconscious from a presumed opioid overdose should still be administered naloxone in the field to avoid maternal death.

- Pregnant women should not be prescribed a benzodiazepine in addition to buprenorphine unless there are compelling medical indications which should be well-documented in the medical record.

- After delivery, additional buprenorphine should be given by the patient's usual buprenorphine prescriber for post-delivery pain instead of short-acting opioids, which will not be very effective due to the buprenorphine blockade of the mu receptors in the brain. For most vaginal deliveries, an extra 2mg of buprenorphine every 4 hours prn pain

for 2 or 3 days is efficacious. After a Cesarean section, an extra 4mg every 4 hours prn for 2-3 days, then an extra 2mg every 4 hours prn for 2-3 days, usually works well. Communication with the obstetrician about this approach is critical to avoid relapse after delivery with the commonly prescribed short-acting opioids.

- Breastfeeding may help reduce the incidence and severity of neonatal abstinence syndrome, and is encouraged in HIV-negative women, provided they are able to remain abstinent from the use of alcohol, benzodiazepines, or other sedating substances.

- Co-sleeping of mother and infant is discouraged due to increased risk of inadvertent infant asphyxiation if the mother becomes sedated from the use of alcohol, benzodiazepines, or other sedating substances.

- There should not be arbitrary time limits on buprenorphine treatment, especially for pregnant women.

Margaret Gregorczyk, MD

References:

1. Neonatal outcomes following in utero exposure to buprenorphine/naloxone or methadone. - PubMed – NCBI https://www.ncbi.nlm.nih.gov/pubmed/26770721
2. Observational study of the safety of buprenorphine+naloxone in pregnancy in a rural and remote population. - PubMed – NCBI https://www.ncbi.nlm.nih.gov/pubmed/27799240
3. Buprenorphine and naloxone compared with methadone treatment in pregnancy. - PubMed - NCBI https://www.ncbi.nlm.nih.gov/pubmed/25569005
4. Buprenorphine + naloxone in the treatment of opioid dependence during pregnancy-initial patient care and outcome data. - PubMed – NCBI https://www.ncbi.nlm.nih.gov/pubmed/23617867

Neonatal Abstinence Syndrome

Neonatal abstinence syndrome (NAS) occurs when a developing fetus is exposed to opiates in utero from a mother who is taking opioid pain relievers, illicit opiates including heroin, or participating in medication-assisted treatment. When born, the infant may exhibit a constellation of symptoms due to physical withdrawal from the opiates and may require pharmacologic management with opiates, morphine or methadone, in addition to non-pharmacologic measures to reduce the severity of the withdrawal.

Over the past decade, the opioid epidemic has worsened across the United States and the effects on the exposed infants were not well understood. The incidence of NAS has increased dramatically over the past decade, from 3.4 infants/1000 deliveries in 2009[1] to 5.8 infants/1000 deliveries in 2012.[2] There are definite regional differences in NAS, with the South Central census division (TN, AL, MS, KY) with rates of 15-20/1000 and New England having rates of 10-15/1000.[2] Current rates of NAS in Virginia are estimated at 6/1000, very close to the national average, but there are concerns that the overall rate may be higher due to under-reporting. National cost estimates for the initial hospitalization of these infants is approximately $93,000 per infant, with an annual total expenditure of greater than $55 million for infants born in Virginia hospitals.

Over the past few years, there has been increased interest in improving the care of infants and families affected by NAS. There have been a few regional neonatal collaboratives[3,4,5] that have worked on

improving the care of infants and families affected by NAS. Desired outcomes include decreased length of stay, decreased number of days of pharmacological treatment and improved breastfeeding rates of NAS infants. These collaboratives introduced many potentially-better practices (PBP's) that have helped shape the development of policies and protocols to standardize the care of these infants.

There have been a few studies evaluating the use of buprenorphine for medication-assisted treatment and its effects on NAS. The MOTHER study which randomized pregnant women to either methadone or buprenorphine treatment for medication-assisted treatment demonstrated a significant reduction in both length of stay and duration of pharmacologic therapy in the buprenorphine group when compared to the methadone group for NAS infants.[7] Additional recent studies have found similar results with a lower length of stay, decreased need for pharmacologic therapy for exposed infants, and lower total morphine exposure for the treated infants.[8,9]

In summary, neonatal abstinence syndrome affects the most vulnerable patients of the Commonwealth of Virginia and its incidence continues to increase each year due to the national opioid epidemic which has touched more and more families in our state. Medication-assisted treatment is the mainstay for all patients with opioid substance disorders, especially pregnant women due to the effects of opioids on the fetus. While methadone may be appropriate for pregnant mothers in certain situations, treatment with buprenorphine is also an accepted therapy which may lessen the effects of NAS on exposed infants. Continued support of these infants and their families with publically available services such as WIC, Early Intervention and developmental follow-up can only help to improve the care of infants and families affected by opiates and NAS.

Alan Picarillo, MD, FAAP

References:

1. Patrick SW, Schumacher RE, Benneyworth BD, Krans EE, McAllister JM, Davis MM. Neonatal abstinence syndrome and associated health care expenditures: United States, 2000-2009. JAMA 2012; 307: 1934-40.
2. Patrick SW, Davis MM, Lehman CU, Cooper WO. Increasing incidence and geographic distribution of neonatal abstinence syndrome: United States 2009 to 2012. Journal of Perinatology (2015), 1–6
3. Hall ES, Wexelblatt SL, Crowley M, et al. OCHNAS Consortium. Implementation of a neonatal abstinence syndrome weaning protocol: a multicenter cohort study. *Pediatrics*. 2015;136(4).
4. Patrick SW, Schumacher RE, Horbar JD, et al. Improving Care for Neonatal Abstinence Syndrome. *Pediatrics*. 2016;137(5):e20153835
5. Massachusetts Neonatal Abstinence Syndrome Improvement Project. Available at: www. neoqic. org/ nasproject. Accessed March 2, 2015
6. http://www.samhsa.gov/medication-assisted-treatment/treatment (accessed 8/20/2016)
7. Jones H, et al. Neonatal Abstinence Syndrome after Methadone or Buprenorphine Exposure. N Engl J Med 2010; 363:2320-2331
8. Hall, Eric S. et al. A Cohort Comparison of Buprenorphine versus Methadone Treatment for Neonatal Abstinence Syndrome The Journal of Pediatrics , Volume 170 , 39 - 44.e1
9. Wiegand, SL et al. Buprenorphine and Naloxone Compared With Methadone Treatment in Pregnancy. Obstetrics & Gynecology; 2015: (20) 363-368.

Adolescents

The use of buprenorphine for the treatment of opioid addiction in adolescents has not been systematically studied. It is known, however, that patients younger than 18 years of age, with relatively short addiction histories, are at particularly high risk for serious complications of addiction, e.g., overdose deaths, suicide, HIV, other infectious diseases. Many experts in the field of opioid addiction treatment believe

that buprenorphine should be the treatment of choice for adolescent patients with short addiction histories. Additionally, buprenorphine may be an appropriate treatment option for adolescent patients who have histories of opioid abuse and addiction and multiple relapses, but who are not currently dependent on opioids. Buprenorphine may be preferred to methadone for the treatment of opioid addiction in adolescents because of the relative ease of withdrawal from buprenorphine treatment.

Because adolescents often present with short histories of drug use, detoxification with buprenorphine followed by drug-free or naltrexone treatment, should be attempted before proceeding to opioid maintenance. Naltrexone may be a valuable therapeutic adjunct after detoxification. Naltrexone has no abuse potential and may help to prevent relapse by blocking the effects of opioids if the patient relapses to opioid use. Naltrexone has been a valuable therapeutic adjunct in some opioid-abusing populations, particularly youth and other opioid users early in the course of addiction. Naltrexone is most likely to be effective for patients with strong support systems that include one or more individuals willing to observe, supervise, or administer the naltrexone on a daily basis. In those adolescent patients in whom detoxification is followed by relapse, buprenorphine maintenance may then be the appropriate alternative. The treatment of patients younger than 18 years of age can be complicated due to psychosocial considerations, the involvement of family members, and Virginia law concerning consent and reporting requirements for minors. (TIP 40)

In Virginia, a minor shall be deemed an adult for the purposes of giving consent to medical or health services needed in the case of outpatient care, treatment or rehabilitation for substance abuse as defined in Section 37.2-100. Adolescent patients, however, should be 16 or older. Buprenorphine is not currently recommended for use in those less than 16 years of age (FDA 2010).

Mark Stevens, MD

Patients with Pain (adapted from TIP 40)

- Patients who need treatment for pain but not for addiction should be treated within the context of their regular medical or surgical setting. They should not be transferred to an opioid maintenance treatment program simply because they are being prescribed an opioid and have become physically dependent on it in the course of their medical treatment.

- It can be difficult to distinguish between the legitimate desire to use opioids for pain relief and the desire to procure them for purposes of diversion or obtaining a high. It is important to remember that the subjective goal of pain relief should be accompanied by objective improvements in functioning. Even patients at the end of a terminal illness will demonstrate improved functioning if their pain is controlled, for example: reviewing their lives, making out a will, conferring with spiritual advisors, "getting their house in order."

- Functional objectives should be keyed to developmental tasks keeping in mind that the achievement of developmental tasks in ALL phases of life is paramount to the happiness and fulfillment of human beings. Adequate pain relief for a 12-month old child should result in his/her learning to walk and beginning to put words together. Adequate pain relief for a young adult should result in forward motion towards independence and would include obtaining employment and forming adult relationships. For most adults, returning to gainful employment is a developmentally appropriate functional goal.

- Functional objectives can be identified, quantified and independently verified if possible. An example of this would be attendance in physical therapy with verification of good effort by the

physical therapist. Even retired individuals can establish measureable goals such as spending more time with grandchildren or actively pursuing hobbies. Family members can be helpful in verifying the achievement of functional goals.

- Failure to achieve functional goals should raise questions about the original diagnoses and the plan of care. Not all pain responds to opioids. Also, the risks of opioids can outweigh their benefits, especially in patients with the disease of addiction.

- In addition to poor functioning, the more obvious signs of harm due to prescribed opioids can not be ignored: overdoses, concomitant use of illicit substances, and diversion. If it becomes evident that the negative effects of opioids outweigh the positives, the opioids should be discontinued. Prescribers should be familiar with how to safely discontinue any medication they prescribe.

Mary McMasters, MD

Patients with Medical Comorbidities

(Adapted from TIP 40 and the Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction http://www.ncbi.nlm.nih.gov/books/NBK64237/)

Patients addicted to opioids who present for treatment often have other comorbid medical problems. These conditions are often a consequence of high-risk behaviors, including injection drug use by intravenous, intramuscular, or subcutaneous routes, mucosal exposure from snorting, or of the direct toxic effects of the active and inert ingredients in illicit drugs. The prevalence of infectious diseases, e.g. HIV/AIDS, hepatitis B and C, tuberculosis, skin and soft tissue infections, syphilis and other sexually transmitted diseases [STDs], is increased in these patients, which should have screening tests. Other comorbid conditions, e.g. seizure disorders, valvular heart disease secondary to talc granulomatosis, lymphedema, pseudo aneurysms of the neck and groin secondary to thrombophlebitis, and renal insufficiency secondary to heroin-associated nephropathy, also are seen in the population and may require special attention. Patients with a history of endocarditis need antibiotic prophylaxis before certain dental procedures. Patients with a history of hepatitis C may require hepatitis A and B vaccinations and may be intolerant of potentially hepatotoxic medications. There have been some reports of elevated liver function tests in patients treated with buprenorphine who also have a history of hepatitis; it is suggested that liver function tests be monitored in these patients on a regular basis during buprenorphine treatment. A detailed discussion of medical comorbidities in addiction is beyond the scope of this chapter and is reviewed extensively in THE ASAM PRINCIPLES OF ADDICTION MEDICINE, 5th edition, Ries, Fiellin, Miller, Saitz, 2014 Wolters-DKluwer.

Treatment of opioid addiction in patients with comorbid medical conditions is likely to result in better outcomes for the comorbid conditions than would be achieved in the absence of treatment of the substance use disorder. However, it is important to remember that treatments of comorbid medical disorders may have important drug interactions with buprenorphine due to shared pharmacokinetic properties. Buprenorphine is metabolized by the hepatic cytochrome P450 3A4 enzyme system and will likely interact with other medications metabolized ty the same system. For example, certain antiretrovirals may occupy the cytochrome P450 3A4 system and thus inhibit the metabolism of buprenorphine. Other drugs that induce the cytochrome P450 3A4 system, e.g. certain antituberculosis, anticonvulsant, and antiretroviral medications, may decrease serum concentrations of buprenorphine, resulting in opioid withdrawal or decreased effectiveness.

Detection of comorbid medical conditions most often occurs during a thorough physical exam with particular attention paid to signs and symptoms common to patients with active addiction.

Laboratory evaluation of patients who are addicted to opioids can also detect comorbid medical conditions. However, obtaining laboratory tests should not delay the appropriate treatment of active addiction, particularly addiction to opioids, due to the high risk of overdose and death in this population.

In summary, it is important to screen for and manage common comorbid medical conditions in patients being treated with buprenorphine for opioid addiction and to anticipate known and potential drug interactions.

Mary McMasters, MD

Geriatrics (from SAMHSA TIP 40)

"Literature on the use of buprenorphine in geriatric patients is extremely limited. Due to potential differences in rates of metabolism and absorption compared to younger individuals, care should be exercised in the use of buprenorphine in geriatric patients. Particular care should be exercised during buprenorphine induction both because of differences in body composition and because of the possibility of medication interactions. "

Kenneth Walker, MD

Patients with Significant Psychiatric Comorbidity (adapted from SAMHSA TIP 40)

The association of psychopathology and opioid addiction is well established. The rate of psychiatric diagnosis in individuals seeking treatment at methadone clinics is approximately 39 percent. Although the etiological significance of psychiatric disorders in the genesis of opioid addiction is not established, it is known that treatment for both conditions is necessary for substance abuse treatment to be effective. Therefore, the presence and severity of comorbid psychiatric conditions must be assessed in patients who are opioid-addicted before, or while, initiating buprenorphine treatment, and a determination must be made whether referral to specialized behavioral health services is indicated. Untreated or inadequately treated psychiatric disorders can interfere with the effective treatment of addiction.

Primary psychiatric disorders may improve but do not dissipate with abstinence or maintenance therapies, and these disorders may require additional treatment. The most commonly encountered psychiatric disorders in opioid-addicted patients are other substance use disorders, depressive disorders, bipolar spectrum disorders, posttraumatic stress disorder, substance-induced psychiatric disorders, and antisocial and borderline personality disorders.

The presence of a psychiatric disorder should not exclude a patient from buprenorphine treatment. However, if there is suicidal or homicidal ideation, symptoms of acute psychosis, or other acute or chronic issues that may render a patient unstable, referral for specialized assessment and treatment is indicated prior to embarking upon buprenorphine treatment.

William L. Harp, MD

Patients Recently Discharged from Controlled Environments (adapted from SAMHSA TIP 40)

Considered here are individuals that have been incarcerated in prison and involuntarily detoxified from opioids, patients discharged from extended hospital or rehab center stays, patients returning from extended overseas travel to countries without access to opioids, and other situations that caused an

involuntary break in the use and addiction to opioids. Assessment of invididuals with these circumstances is to determine if they will resume their addiction if not treated with buprenorphine.

The following factors should be part of the assessment: length of incarceration, post-release addiction patterns and cycles, addiction treatment history, self-help involvement, reported triggers of illegal drug use and addiction upon release, comorbid psychiatric issues, and the patient's level of commitment to treatment and the likelihood of self-control.

Psychosocial issues that should be assessed are the number and length of incarcerations, types of crimes committed, gang affiliations, type and length of parole or probation, the patient's collateral contacts and reporting requirements, prior and current opioid abuse problems in the family, recent familiar or marital relationships, whether permission from the criminal justice system is required for treatment with buprenorphine, and the plan for a stable lifestyle.

The decision to treat will be based upon the patient's medical history, subjective report, the risk of diversion and overdose, the ability of the physician and treatment to have an impact, cost and other considerations.

Section IV: Definitions

Accurate use of terminology is essential to understanding office-based treatment of opioid addiction [70]. However, terminology in this area is changing. For many years, the most commonly used terms have been "drug abuse" and "drug dependence," with the latter indicating a severe condition considered synonymous with the term "addiction" (the chronic brain disease). The terms "abuse" and "dependence," in use since the third edition of the *Diagnostic and Statistical Manual of Mental Disorders* [79] has been replaced in the fifth edition [80] by the term "substance use disorder." Other new terms include "opioid use disorder" for the activity of using opioids benignly or pathologically, and "opioid use disorder" for the disease associated with compulsive, out-of-control use of opioids.

For the purposes of this Model Policy, the following terms are defined as shown.

Abuse: The definition of "abuse" varies widely, depending on the context in which it is used and who is supplying the definition. The Code of Virginia defines "substance abuse" as the use of drugs or alcohol that results in dependence, danger to self or others, mental, emotional or phsycial impairment that causes dysfunctional behavior. The *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, of the American Psychiatric Association defines "substance use disorders" as "a cluster of cognitive, behavioral, and physiological symptoms indicating that the individual continues using the substance despite significant substance-related problems."

Addiction: Addiction is widely defined as a primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include the following: impaired control over drug use, craving, compulsive use, and continued use despite harm [56]. (As discussed below, physical dependence and tolerance are normal physiological consequences of extended opioid therapy and are not the same as addiction.)

A recent definition of addiction, adopted by the American Society of Addiction Medicine in 2011, reads as follows: "Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors. Addiction is characterized by inability to consistently abstain,

impairment in behavioral control, craving, diminished recognition of significant problems with one's behaviors and interpersonal relationships, and a dysfunctional emotional response. Like other chronic diseases, addiction often involves cycles of relapse and remission. Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death" [82].

Controlled Substance: In Virginia, the definition of a "controlled substance" means a drug, substance or immediate precursor in Schedules I through VI.

The federal definition of a "controlled substance" is a drug that is subject to special requirements under the federal Controlled Substances Act [75], which is designed to ensure both the availability and control of regulated substances. Under the CSA, availability of regulated drugs is accomplished through a system that establishes quotas for drug production and a distribution system that closely monitors the importation, manufacture, distribution, prescribing, dispensing, administering, and possession of controlled drugs [83]. Civil and criminal sanctions for serious violations of the statute are part of the government's drug control apparatus. The Code of Federal Regulations (Title 21, Chapter 2) implements the CSA.

The CSA [75], confers responsibility for scheduling controlled substances on the FDA and the DEA. In granting regulatory authority to these agencies, the Congress noted that both public health and public safety needs are important and that neither takes primacy over the other, but that both are necessary to ensure the public welfare. To accomplish this, the Congress provided guidance in the form of factors that must be considered by the FDA and DEA when assessing public health and safety issues related to a new drug or one that is being considered for rescheduling or removal from control.

Most opioids are classified as Schedule II or III drugs under the CSA, indicating that they have a high potential for abuse and a currently accepted medical use in treatment in the U.S., and that abuse of the drug may lead to psychological or physical dependence [75]. (Although the scheduling system provides a rough guide to abuse potential, it should be recognized that all controlled substances have some potential for abuse.)

Dependence: Physical dependence is a state of biologic adaptation that is evidenced by a class-specific withdrawal syndrome when the drug is abruptly discontinued or the dose rapidly reduced, and/or by the administration of an antagonist [76]. It is important to distinguish addiction from the type of physical dependence that can and does occur within the context of good medical care, as when a patient on long-term opioid analgesics for pain becomes physically dependent on the analgesic. This distinction is reflected in the two primary diagnostic classification systems used by health care professionals: the *International Classification of Mental and Behavioural Disorders, 10th Edition* (*ICD-10*) of the World Health Organization (WHO) [84] and the *Diagnostic and Statistical Manual (DSM)* of the American Psychiatric Association [80,81]. In the DSM-IV-TR, a diagnosis of "substance dependence" meant addiction. In the upcoming DSM V, the term *dependence* is reestablished in its original meaning of physiological dependence; when symptoms are sufficient to meet criteria for substance misuse or addiction, the term "substance use disorder" is used, accompanied by severity ratings [80].

It may be important to clarify this distinction during the informed consent process, so that the patient understands that physical dependence and tolerance are likely to occur if opioids are taken regularly for a period of time, but the risk of addiction is relatively low unless the patient has additional risk factors. According to the World Health Organization, "The development of tolerance and physical dependence denote normal physiologic adaptations of the body to the presence of an opioid" [8].

Detoxification: Detoxification (also termed "medically supervised withdrawal") refers to a gradual reduction, or tapering, of a medication dose over time, under the supervision of a physician, to achieve the elimination of tolerance and physical dependence [85].

"Detoxification" is a legal and regulatory term that has fallen into disfavor with some in the medical community; indeed, some experts view "detoxification" as a misnomer because many abusable drugs are not toxic when administered in proper doses in a medical environment [86].

Diversion: The federal Controlled Substances Act (21 U.S.C. §§ 801 et seq.) establishes a closed system of distribution for drugs that are classified as controlled substances. Records must be kept from the time a drug is manufactured to the time it is dispensed. Health care professionals who are authorized to prescribe, dispense, and otherwise control access to such drugs are required to register with the DEA [75].

Pharmaceuticals that make their way outside this closed system are said to have been "diverted" from the system, and the individuals responsible for the diversion (including patients) are in violation of the law. The degree to which a prescribed medication is misused depends in large part on how easily it is redirected (diverted) from the legitimate distribution system [30,87].

Maintenance Treatment: Maintenance treatment involves the dispensing or administration of an opioid medication (such as methadone or buprenorphine) at a stable dose and over a period of 21 days or more, for the treatment of opioid addiction. When maintenance treatment involves the use of methadone, such treatment must be delivered in an Opioid Treatment Program (OTP). However, maintenance treatment with buprenorphine may be delivered in either an OTP or a medical office by a properly credentialed physician [7].

Medication-Assisted Treatment (MAT): MAT is any treatment for opioid addiction that includes a medication (such as methadone, buprenorphine, or naltrexone) that is approved by the FDA for opioid detoxification or maintenance treatment. MAT may be provided in a specialized OTP or, for buprenorphine or naltrexone, in a physician's office or other health care setting [7,55].

Misuse: The term *misuse* (also termed *non-medical use*) incorporates all uses of a prescription medication other than those that are directed by a physician and used by a patient within the law and the requirements of good medical practice [56].

Opioid: An opioid is any compound that binds to an opioid receptor. The class includes both naturally occurring and synthetic or semi-synthetic opioid drugs or medications, as well as endogenous opioid peptides [7,51,83]. Most physicians use the terms "opiate" and "opioid" interchangeably, but toxicologists (who perform and interpret drug tests) make a clear distinction between them. "Opioid" is the broader, more appropriate term because it includes the entire class of agents that act at opioid receptors in the nervous system, whereas "opiates" refers to natural compounds derived from the opium plant but not semisynthetic opioid derivatives of opiates or completely synthetic agents. Thus, drug tests that are "positive for opiates" have detected one of these compounds or a metabolite of heroin, 6-monoacetyl morphine (MAM); drug tests that are "negative for opiates" have found no detectable levels of opiates in the sample, even though other opioids that were not tested for, including the most common currently used and misused prescription opioids, may well be present in the sample that was analyzed.

Opioid agonists are compounds that bind to the mu opioid receptors in the brain, producing a response that is similar in effect to the natural ligand that would activate it. With full mu opioid agonists, increasing the dose produces a more intense opioid effect. Most opioids that are misused, such as morphine and heroin, are full mu opioid agonists, as is methadone.

Opioid partial agonists occupy and activate the opioid receptors, but the activation they produce reaches a plateau, beyond which additional opioid doses do not produce a greater effect. It should be noted that the plateau (or "ceiling effect") may limit a partial agonist's therapeutic activity as well as its toxicity. Buprenorphine is a partial mu opioid agonist.

Opioid antagonists bind to and block the opioid receptors and prevent them from being activated by an opioid agonist or partial agonist. Naltrexone and naloxone both are opioid antagonists, and both can block the effect of opioid drugs.

Opioid Treatment Program *(OTP)* (sometimes referred to as a "methadone clinic" or "narcotic treatment program"): An OTP is any treatment program certified by SAMHSA in conformance with 42 Code of Federal Regulations (CFR), Part 8, to provide supervised assessment and medication-assisted treatment of patients who are addicted to opioids. An OTP can exist in a number of settings, including intensive outpatient, residential, and hospital facilities. Treatments offered by OTPs include medication-assisted therapy with methadone, buprenorphine or naltrexone, as well as medically supervised withdrawal or detoxification, accompanied by varying levels of medical and psychosocial services and other types of care. Some OTPs also can provide treatment for co-occurring mental disorders [58].

Recovery: A process of change through which individuals improve their health and wellness, live a self-directed life, and strive to reach their full potential [88]. As used in the ASAM *Patient Placement Criteria*, "recovery" refers to the overall goal of helping a patient achieve overall health and well-being [56]. SAMHSA's 10 guiding principles recognize that recovery [89]:

- Emerges from hope;
- Is person-driven;
- Occurs via many pathways;
- Is holistic;
- Is supported by peers and allies;
- Is supported through relationship and social networks
- Is culturally-based and influenced;
- Is supported by addressing trauma;
- Involves individual, family and community strengths and responsibility;
- Is based on respect.

Relapse: Relapse has been variously defined as "a breakdown or setback in a person's attempt to change or modify any target behavior" and as "an unfolding process in which the resumption of substance misuse is the last event in a long series of maladaptive responses to internal or external stressors or stimuli" [70]. Relapse rarely is caused by any single factor and often is the result of an interaction of physiologic and environmental factors [59].

The term *lapse* (sometimes referred to as a *slip*) refers to a brief episode of drug use after a period of abstinence. A lapse usually is unexpected, of short duration, with relatively minor consequences, and marked by the patient's desire to return to abstinence. However, a lapse also can progress to a full-blown relapse, marked by sustained loss of control [56].

Tolerance: Tolerance is a state of physiologic adaptation in which exposure to a drug induces changes that result in diminution of one or more of the drug's effects over time [76]. Tolerance may occur both to an opioid's analgesic effects and to its unwanted side effects, such as respiratory depression, sedation, or nausea. Most investigators agree that absolute tolerance to the analgesic effects of opioids does not occur.

In general, tolerance to the side effects of opioids develops more rapidly than does tolerance to the drug's analgesic effects.

Tolerance may or may not be evident during treatment with opioids and is not the same as addiction [70].

Trial Period: A period of time, which can last weeks or even months, during which the efficacy of a medication or other therapy for the treatment of addiction is tested to determine whether the treatment goals can be met. If the goals are not met, the trial should be discontinued and an alternative approach (i.e., a different medication or non-pharmacologic therapy) adopted [76].

Waiver: A documented authorization from the Secretary of Health and Human Services, issued by SAMHSA under the DATA 2000 regulations, that exempts a qualified physician from the rules applied to OTPs and allows him or her to use buprenorphine for the treatment of addiction in office-based practice [51].

References

1. Office of National Drug Control Policy (ONDCP). *Epidemic: Responding to America's Prescription Drug Abuse Crisis.* Washington, DC: ONDCP, Executive Office of the President, The White House, 2011.

2. Becker WC, Sullivan LE, Tetrault JM et al. Non-medical use, abuse and dependence on prescription opioids among U.S. adults: Psychiatric, medical and substance use correlates. *Drug and Alcohol Dependence.* 2008 Apr 1;94(1-3):38-47.

3. Arfken CL, Johanson CE, diMenza S et al. Expanding treatment capacity for opioid dependence with buprenorphine: National surveys of physicians. *Journal of Substance Abuse Treatment.* 2010 Sep;39(2):96-104.

4. Gunderson EW & Fiellin DA. Office-based maintenance treatment of opioid dependence: How does it compare with traditional approaches? *CNS Drugs* 2008;22(2):99-111.

5. National Institute on Drug Abuse (NIDA). *Topics in Brief: Medication-Assisted Treatment for Opioid Addiction.* Bethesda, MD: NIDA, National Institutes of Health, April 2012.

6. Korthuis PT, Gregg J, Rogers WE et al. Patients' reasons for choosing office-based buprenorphine: Preference for patient-centered care. *Journal of Addiction Medicine.* 2010;4(4):204-210.

7. McNicholas LF, chair, for the CSAT Expert Panel. *Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction.* Treatment Improvement Protocol [TIP] Series Number 40. DHHS Publication No. [SMA] 04-3939. Rockville, MD: Center for Substance Abuse Treatment, Substance Abuse and Mental Health Services Administration, 2004.

8. World Health Organization (WHO). *Guidelines for the Psychologically Assisted Pharmacological Treatment of Opioid Dependence.* Geneva, Switzerland: WHO, 2009.

9. Soyka M, Kranzler HR, Van den Brink W et al. The World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for the Biological Treatment of Substance Use and Related Disorders—Part 2: Opioid Dependence. *World Journal of Biological Psychiatry.* 2011 Apr;12(3):160-187.

10. Community Care Behavioral Health (CCBH) & Institutes for Research Education and Training in Addictions (IRETA). *Buprenorphine Treatment for Opioid Dependence.* Pittsburgh, PA: CCBH & IRETA, May 2011.

11. O'Connor PG. Advances in the treatment of opioid dependence: Continued progress and ongoing challenges. *Journal of the American Medical Association.* 2010;304:1612-1614.

12. Amato L, Davoli M, Perucci CA et al. An overview of systematic reviews of the effectiveness of opiate maintenance therapies: Available evidence to inform clinical practice and research. *Journal of Substance Abuse Treatment* 2005; 28:321-329.

13. Umbricht A, Huestis M, Cone EJ et al. Effects of high-dose intravenous buprenorphine in experienced opioid abusers. *Journal of Clinical Psychopharmacology.* 2004 Oct;24(5):479-487.

14. Teesson M, Ross J, Darke S et al. One year outcomes for heroin dependence: Findings from the Australian Treatment Outcome Study (ATOS). *Drug and Alcohol Dependence.* 2006 Jun 28;83(2):174-180.

15. Ducharme S, Fraser R, Gill K. Update on the clinical use of buprenorphine in opioid-related disorders. *Canadian Family Physician.* 2012 Jan;58(1):37-41.

16. Gordon AJ, Kunins HV, Rastegar DA et al. Update in addiction medicine for the generalist. *Journal of General Internal Medicine.* 2011;26(1):77-82.

17. Chiang CN & Hawks RL. Pharmacokinetics of the combination tablet of buprenorphine and naloxone. *Drug and Alcohol Dependence.* 2003;70:S39-S47.

18. Bauer SM, Loipl R, Jagsch R et al. Mortality in opioid-maintained patients after release from an addiction clinic. *European Addiction Research.* 2008;14(2):82-91.

19. Gibson AE, Degenhardt LJ, Mattick RP et al. Exposure to opioid maintenance treatment reduces long-term mortality. *Addiction.* 2008;103(3):462-468.

20. Nielsen S, Dietze P, Lee N et al. Concurrent buprenorphine and benzodiazepines use and self-reported opioid toxicity in opioid substitution treatment. *Addiction.* 2007 Apr;102(4):616-622.

21. Sporer KA. Buprenorphine: A primer for emergency physicians. *Annals of Emergency Medicine.* 2004 May;43(5):580-584. Review.

22. Auriacombe M, Lagier G, Mallaret M et al. *French experience with buprenorphine.* In WL Dewey, LS Harris (eds.) *Problems of Drug Dependence, 2002: Proceedings of the 64th Annual Scientific Meeting, The College on Problems of Drug Dependence.* NIDA Research Monograph. 183. National Institutes of Health (NIH) Publication No. 03–5339.Rockville, MD: National Institute on Drug Abuse., 2003.

23. Boyer EW, McCance-Katz EF, Marcus S. Methadone and buprenorphine toxicity in children. *American Journal of Addiction.* 2010 Jan-Feb;19(1):89-95

24. Seet RC, Rathakrishnan R, Chan BP et al. Diffuse cystic leukoencephalopathy after buprenorphine injection. *Journal of Neurology, Neurosurgery and Psychiatry.* 2005 Jun;76(6):890-891.

25. Loo HW, Yam AK, Tan TC et al. Severe upper limb complications from parenteral abuse of Subutex. *Annals of the Academy of Medicine of Singapore.* 2005 Oct;34(9):575-578.

26. Albotins CA, Allen P, Daffy JR. Fungal endophthalmitis in intravenous drug users injecting buprenorphine contaminated with oral Candida species (Letter). *Medical Journal of Australia.* 2005;182(8):427.

27. Etchepare F, Coutaux A, Edel Y et al. Enterobacter cloacae spondylodiscitis through misuse of high dose intravenous buprenorphine. *Presse Medicine.* 2005; 34(10):725-727.

28. Cazorla C, Grenier de Cardenal D, Schumacher H et al. Infectious complications and misuse of high-dose buprenorphine. *Presse Medicine.* 2005; 34(10):719-724.

29. Diguisto E, Shakeshaft A, Ritter A et al. Serious adverse events in the Australian National Evaluation of Pharmacotherapies for Opioid Dependence (NEPOD). *Addiction* 2004;99(4):450–460.

30. Johnson CE, Arfken CL, DiMenza S et al. Diversion and abuse of buprenorphine: Findings from national surveys of treatment patients and physicians. *Drug and Alcohol Dependence.* 2012 Jan 1;120(1-3):190-195.

31. Maxwell JC & Wilford BB, for the Substance Abuse and Mental Health Services Administration. *Diversion and Abuse of Buprenorphine: A Brief Assessment of Emerging Indicators. Final Report.* Silver Spring, MD: JBS International, Inc., 2006.

32. Jaffe JH & O'Keeffe C. From morphine clinics to buprenorphine: Regulating opioid agonist treatment of addiction in the United States. *Drug and Alcohol Dependence.* 2003 May 21;70(2 Suppl):S3-11.

33. Dasgupta N, Kramer ED, Zalman MA et al. Association between non-medical and prescriptive usage of opioids. *Drug and Alcohol Dependence.* 2006 Apr 28;82(2):135-142.

34. Bazazi AR, Yokell M, Fu JJ et al. Illicit use of buprenorphine/naloxone among injecting and noninjecting opioid users. *Journal of Addiction Medicine.* 2011 Sep;5(3):175-180.

35. Johansen CE, Arfken CL, di Menza S et al. Diversion and abuse of buprenorphine: findings from national surveys of treatment patients and physicians. *Drug and Alcohol Dependence.* 2012 Jan 1;120(1-3):190-195.

36. Lofwall MR & Havens JR. Inability to access buprenorphine treatment as a risk factor for using diverted buprenorphine. *Drug and Alcohol Dependence.* 2012 Dec 1;126(3):379-383.

37. Federation of State Medical Boards (FSMB). *Model Policy on Opioid Addiction Treatment in the Medical Office.* Dallas, TX: The Federation, 2002

38. O'Brien CP. Toward a rational selection of treatment for addiction. *Current Psychiatry Reports.* 2007 Dec;9(6):441-442.

39. Salsitz EA & Wunsch MJ, for the Physician Clinical Support System for Buprenorphine (PCSS-B). *PCSS-B Guidance on Drug Enforcement Administration Requirements for Prescribers and Dispensers of Buprenorphine and Buprenorphine/Naloxone.* East Providence, RI: American Academy of Addiction Psychiatry, January 25, 2010.

40. Bruce RD. Medical interventions for addictions in the primary care setting. *Topics in HIV Medicine.* 2010 Feb-Mar;18(1):8-12.

41. Barry DT, Irwin KS, Jones ES et al. Integrating buprenorphine treatment into office-based practice: A qualitative study. *Journal of General Internal Medicine.* 2009 Feb;24(2):218-225.

42. Jones ES, Moore BA, Sindelar JL et al. Cost analysis of clinic and office-based treatment of opioid dependence: Results with methadone and buprenorphine in clinically stable patients. *Drug and Alcohol Dependence.* 2009 Jan 1;99(1-3):132-140.

43. Fiellin DA , Moore BA, Sullivan LE et al. Long-term treatment with buprenorphine/naloxone in primary care: Results at 2-5 years. *American Journal on Addiction.* 2008 Mar-Apr;17(2):116-120.

44. Sullivan LE & Fiellin DA. Narrative review: Buprenorphine for opioid-dependent patients in office practice. *Annals of Internal Medicine.* 2008 May 6;148(9):662-670. Review.

45. Walley AY, Alperen JK, Cheng DM et al. Office-based management of opioid dependence with buprenorphine: Clinical practices and barriers. *Journal of General Internal Medicine.* 2008 Sep; 23(9):1393-1398.

46. Finch JW, Kamien JB & Amass L. Two-year experience with buprenorphine-naloxone (Suboxone) for maintenance treatment of opioid dependence within a private practice setting. *Journal of Addiction Medicine* 2007 Jun;1(2):104-110.

47. Magura S, Lee SJ, Salsitz EA et al.. Outcomes of buprenorphine maintenance in office-based practice. *Journal of Addictive Diseases.* 2007;26(2):13-23.

48. Torrington M, Domier CP, Hillhouse M et al. Buprenorphine 101: Treating opioid dependence with buprenorphine in an office-based setting. *Journal of Addictive Diseases.* 2007;26(3):93-99.

49. Gordon AJ, Krumm M, for the Buprenorphine Initiative in the VA (BIV). *Buprenorphine Resource Guide, Version 8.* Washington, DC: Department of Veterans Affairs, April 2008.

50. Meier BR & Patkar AA. Buprenorphine treatment: Factors and first-hand experiences for providers to consider. *Journal of Addictive Diseases.* 2007;26(1).

51. Drug Addiction Treatment Act of 2000 (DATA). *Federal Register* (CFR). Public Law No. 106-310, Title XXXV, Section 3501 and 3502.

52. Alford DP, LaBelle CT, Kretsch N et al. Collaborative care in opioid-addicted patients in primary care using buprenorphine. *Archives of Internal Medicine.* 2011;171(5):425-431.

53. Kraus ML, Alford DP, Kotz MM et al. Statement of the American Society of Addiction Medicine Consensus Panel on the Use of Buprenorphine in Office-Based Treatment of Opioid Addiction. *Journal of Addiction Medicine.* 2011 Dec;5(4):254-263.

54. Gourlay D, Heit HA & Caplan Y. *Urine Drug Testing in Clinical Practice.* Stamford, CT: PharmaCom Group, Inc., for the American Academy of Family Physicians, 2010.

55. Amato L, Minozzi S, Davoli M et al. Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification. *Cochrane Database System Review.* 2011 Sept 7;(9):CD005031.

56. Fishman MJ, Mee-Lee D, Shulman GD et al., eds. *Supplement to the ASAM Patient Placement Criteria on the Management of Alcohol Use Disorders.* Baltimore, MD: Lippincott, Williams & Wilkins, Inc., 2010.

57. Lingford-Hughes AR, Welch S, Peters L et al., for the British Association for Psychopharmacology (BAP) Expert Reviewers Group. BAP updated guidelines: Evidence-based guidelines for the pharmacological management of substance abuse, harmful use, addiction and comorbidity: Recommendations from BAP. *Journal of Psychopharmacology.* 2012 July;26(7):899-952.

58. Center for Substance Abuse Treatment (CSAT). *Substance Abuse: Administrative Issues in Outpatient Treatment.* Treatment Improvement Protocol [TIP] 46. Rockville, MD: CSAT, Substance Abuse and Mental Health Services Administration, 2006.

59. McNicholas L. Clinical guidelines for the use of buprenorphine in the treatment of opioid addiction. *A Tool for Buprenorphine Care.* 2008 May;1(12):12.

60. Gunderson EW, Levin FR, Rombone MM et al. Improving temporal efficiency of outpatient buprenorphine induction. *American Journal on Addiction.* 2011;20:397-404..

61. Baxter LE, chair, for the ASAM Methadone Action Group. *Clinical Guidance on Methadone Induction and Stabilization.* Chevy Chase, MD: American Society of Addiction Medicine, Inc., in press 2013.

62. Joseph H, Stancliff S, Lagrod J. Methadone maintenance treatment (MMT): A review of historical and clinical issues. *Mt Sinai Journal of Medicine.* 2000 Oct-Nov;67(5-6):347-64. Review.

63. Marsch LA, Bickel WK, Badger GJ, Jacobs EA. Buprenorphine treatment for opioid dependence: The relative efficacy of daily, twice and thrice weekly dosing. *Drug and Alcohol Dependence.* 2005 Feb 14;77(2): 195-204.

64. Fareed A, Vayalapalli S, Casarella A et al. Effect of buprenorphine dose on treatment outcome. *Journal of Addictive Diseases.* 2012;31(1):8-18

65. Anton RF, O'Malley SS, Ciraulo DA et al., for the COMBINE Study Research Group. Combined pharmacotherapies and behavioral interventions for alcohol dependence: the COMBINE study: A randomized controlled trial. *Journal of the American Medical Association.* 2006 May 3;295(17):2003-2017.

66. Gordon AJ, Trafton JA, Saxon AJ et al., for the Buprenorphine Work Group of the Substance Use Disorders Quality Enhancement Research Initiative. Implementation of buprenorphine in the Veterans Health Administration: Results of the first 3 years. *Drug and Alcohol Dependence.* 2007 Oct 8;90(2-3):292-296.

67. Stotts AL, Dodrill CL & Kosten TR. Opioid addiction treatment: Options in pharmacotherapy. *Expert Opinions in Pharmacotherapy.* 2009 Aug;10(11):1727-1740.

68. Fiellin DA, Kleber H, Trumble-Hejduk JG et al. Consensus statement on office-based treatment of opioid dependence using buprenorphine. *Journal of Substance Abuse Treatment.* 2004;27:153-159.

69. Fiellin DA, Friedland GH & Gourevitch MN. Opioid dependence: Rationale for and efficacy of existing and new treatments. *Clinics of Infectious Diseases.* 2006 Dec 15;43(Suppl)4:S173-177. Review.

70. Heit HA. Addiction, physical dependence, and tolerance: Precise definitions to help clinicians evaluate and treat chronic pain patients. *Journal of Pain and Palliative Care Pharmacotherapy* 2003;17(1):15-29.

71. Marlatt G & Gordon JR, eds. *Relapse Prevention: Maintenance Strategies in the Treatment of Addictive Behaviors.* New York, NY: Guilford Press, 1985.

72. Fareed A, Vayalapalli S, Byrd-Sellers J et al. Safety and efficacy of long-term buprenorphine maintenance treatment. *Addictive Disorders & Their Treatment.* 2011 Sep;10(3):123-130.

73. Batki SL, Kauffman JF, Martion I et al., eds. *Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs.* Treatment Improvement Protocol [TIP] 43. Rockville, MD: Center for Substance Abuse Treatment, Substance Abuse and Mental Health Services Administration, 2005.

74. Stephenson DK, for the CSAM Committee on Treatment of Opioid Dependence. *Draft Guidelines for Physicians Working in California Opioid Treatment Programs.* San Francisco, CA: California Society of Addiction Medicine, 2008.

75. Controlled Substances Act of 1970 (CSA). *Federal Register* (CFR). Public Law No. 91-513, 84 Stat. 1242.

76. Utah Department of Health (UDOH). *Utah Clinical Guidelines on Prescribing Opioids for Treatment of Pain.* Salt Lake City, UT: The Department, February 2009.

77. Alliance for Model State Drug Laws (AMSDL). State Prescription Monitoring Statutes and Regulations Citation List. Alexandria, VA: The Alliance, 2006.

78. Brushwood DB. Maximizing the value of electronic prescription monitoring programs. *Journal of Law, Medicine & Ethics* 2003;31:41-54.

79. American Psychiatric Association (APA). *Diagnostic and Statistical Manual of Mental Disorders, Third Edition (DSM-III).* Washington, DC: American Psychiatric Publishing, Inc., 1980.

80. American Psychiatric Association (APA). *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V).* Washington, DC: American Psychiatric Publishing, Inc., 2013.

81. American Psychiatric Association (APA). *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition-Text Revision (DSM-IV-TR).* Washington, DC: American Psychiatric Publishing, Inc., 2000.

82. American Society of Addiction Medicine (ASAM). Definition of Addiction. Chevy Chase, MD: ASAM, 2011.

83. Drug Enforcement Administration (DEA). Office of Diversion Control. *Physician's Manual: An Informational Outline of the Controlled Substances Act of 1970.* Washington, DC: DEA, U.S. Department of Justice, 1990.

84. World Health Organization (WHO). *International Classification of Diseases, 10th Edition* (ICD-10). Geneva, Switzerland: WHO, 1996.

85. Amato L, Minozzi S, Davoli M et al. Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification. *Cochrane Database System Review.* 2008a Oct 8;(4):CD005031.

86. Center for Substance Abuse Treatment (CSAT). *Guidelines for the Accreditation of Opioid Treatment Programs, Revised.* Rockville, MD: CSAT, Substance Abuse and Mental Health Services Administration, July 20, 2007.

87. Cicero TJ & Inciardi JA. Potential for abuse of buprenorphine in office-based treatment of opioid dependence. *New England Journal of Medicine.* 2005;353(17):1863-1865.

88. White W. Addiction recovery: Its definition and conceptual boundaries. *Journal of Substance Abuse Treatment.* 2007;33:229–241.

89. Substance Abuse and Mental Health Services Administration (SAMHSA). *SAMHSA's Working Definition of Recovery: 10 Guiding Principles of Recovery.* PEP12-RECDEF. Rockville, MD: SAMHSA, 2012.

Model Policy on DATA 2000 and Treatment of Opioid Addiction in the Medical Office

Participation by federal agency representatives and third parties was in an advisory capacity only and does not imply endorsement of any draft or final version of the policy

Chair
Janelle Rhyne, M.D.
Former Board Chair
Federation of State Medical Boards
Cape Fear Health Net Health Net Clinic
Wilmington, North Carolina

Medical Board Representatives
Alfred (Al) Anderson, M.D.
Member, Minnesota Board of Medicine
Medical Pain Management Ltd.
St. Louis Park, Minnesota

J. Daniel Gifford, M.D.
Member, Alabama Board of Medicine
Nephrology of North Alabama
Decatur, Alabama

William L. Harp, M.D.
Executive Director
Virginia Board of Medicine
Richmond, Virginia

Lynn S. Hart
Executive Director
New Mexico Medical Board
Santa Fe, New Mexico

Stancel M. Riley, M.D.
Executive Director
Massachusetts Board of Registration in Medicine
Wakefield, Massachusetts

Joel B. Rose, D.O.
Member, Florida Board of Osteopathic Medicine
Tampa, Florida

Dana Shaffer, D.O.
Member, Iowa Board of Medicine
Exira, Iowa

C. Michael Sheppa, M.D.
Associate Medical Director
North Carolina Medical Board
Chapel Hill, North Carolina

Rosaire Verna, M.D.
Member, Maryland Board of Physicians
Easton, Maryland

Advisors to the Work Group
James W. Finch, M.D.
Director of Physician Education
Governor's Institute on Alcohol and Drug Abuse, and
Medical Director, Changes by Choice, Inc.
Durham, North Carolina

Laura McNicholas, M.D., Ph.D.
Clinical Associate Professor of Psychiatry
University of Pennsylvania and
Veterans Administration Medical Center
Philadelphia, Pennsylvania

Eric C. Strain, M.D.
Professor and Medical Director
Behavioral Pharmacology Research Unit, and
Director, Johns Hopkins Center for
Substance Abuse Treatment and Research
Johns Hopkins University School of Medicine
Baltimore, Maryland

Stephen A. Wyatt, D.O.
Medical Director, Dual Diagnosis Program
Middlesex Hospital
Old Lyme, Connecticut

Federal Agency Representatives
H. Westley Clark, M.D., J.D., M.P.H., CAS, FASAM
Director, Center for Substance Abuse Treatment
Substance Abuse and Mental Health Services
Administration
Rockville, Maryland

Cathy A. Gallagher
Office of Diversion Control
Drug Enforcement Administration
Arlington, Virginia

Sharon Hertz, M.D.
Deputy Director
Division of Anesthesia, Analgesia, and
Rheumatology Products
Food and Drug Administration
Silver Spring, Maryland

Regina LaBelle
Deputy Chief of Staff for Policy
Office of National Drug Control Policy
Executive Office of the President, The White House
Washington, DC

Robert Lubran, M.S., M.P.A.
Director, Division of Pharmacologic Therapies
Center for Substance Abuse Treatment
Substance Abuse and Mental Health Services Administration
Rockville, Maryland

Sandrine Pirard, M.D., Ph.D., M.P.H.
Medical Advisor, Division of Pharmacologic Therapies
Center for Substance Abuse Treatment
Substance Abuse and Mental Health Services Administration
Rockville, Maryland

Nicholas Reuter, M.P.H.
Team Leader, Certification and Waiver Team
Division of Pharmacologic Therapies
Center for Substance Abuse Treatment
Substance Abuse and Mental Health Services Administration
Rockville, Maryland

Alina Salvatore, R.Ph., M.A.
Public Health Advisor, Division of Pharmacologic Therapies
Center for Substance Abuse Treatment
Substance Abuse and Mental Health Services Administration
Rockville, Maryland

Project Staff: FSMB
Lisa A. Robin
Chief Advocacy Officer
Federation of State Medical Boards
Washington, DC

Project Staff: JBS International
Bonnie B. Wilford, M.S.
Director, Center for Health Services & Outcomes Research
and Senior Principal, JBS International, Inc.
North Bethesda, Maryland

Field Reviewers
Chinazo O. Cunningham, M.D., M.S.
(*for the Association for Medical Education and Research in Substance Abuse: AMERSA*)
Associate Professor
Department of Family and Social Medicine
Albert Einstein College of Medicine and Montefiore Medical Center
Bronx, New York

David A. Fiellin, M.D.
Professor of Medicine, Investigative Medicine and Public Health
Yale University School of Medicine
New Haven, Connecticut

Michael H. Gendel, M.D.
(*for the American Academy of Addiction Psychiatry: AAAP*)
Private Practice of Psychiatry
Denver, Colorado

Judith A. Martin, M.D.
(*for the California Society of Addiction Medicine: CSAM*)
Deputy Medical Director, Community Behavioral Health Services,
and Medical Director of Substance Abuse Services
Department of Public Health
City and County of San Francisco, California

William Morrone, D.O., M.S.
(*for the American Academy of Osteopathic Addiction Medicine: AOAAM*)
Department of Family Medicine
Central Michigan University
Saginaw, Michigan

Jennifer McNeely, M.D., M.S.
(*for the Society of General Internal Medicine Substance Abuse Interest Group: SGIM*)
Division of General Internal Medicine
New York University School of Medicine
New York, New York

Michael M. Miller, M.D., FASAM, FAPA
Past President, American Society of Addiction Medicine
Medical Director, Herrington Recovery Center
Rogers Memorial Hospital
Oconomowoc, Wisconsin

William Morrone, D.O., M.S.
(*for the American Academy of Osteopathic Addiction Medicine: AOAAM*)
Department of Family Medicine
Central Michigan University
Saginaw, Michigan

John D. Patz, D.O., FAAFP, FASAM, ABAM
(*for the American Academy of Osteopathic Addiction Medicine: AOAAM*)
Behavioral Health Unit
PRMC Everett
Everett, Washington

Darius A. Rastegar, M.D.
(for the Society of General Internal Medicine Substance Abuse Interest Group: SGIM)
Associate Professor of Medicine
Johns Hopkins University School of Medicine
Baltimore, Maryland

John A. Renner, Jr., M.D.
(for the American Psychiatric Association: APA)
Associate Professor of Psychiatry
Boston University School of Medicine
Boston, Massachusetts

Richard N. Rosenthal, M.D.
(for the American Academy of Addiction Psychiatry: AAAP)
Arthur J. Antenucci Professor of Clinical Psychiatry
Chairman, Department of Psychiatry
St. Luke's Roosevelt Hospital Center, and
Senior Associate Dean for the St. Luke's Roosevelt Hospital Affiliation
New York, New York

Andrew J. Saxon, M.D.
(for the American Psychiatric Association: APA)
Department of Psychiatry
University of Washington Puget Sound
Seattle, Washington

Joanna L. Starrels, M.D., M.S.
(for the Association for Medical Education and Research in Substance Abuse: AMERSA)
Division of General Internal Medicine
Albert Einstein College of Medicine
and Montefiore Medical Center
Bronx, New York

Jeanette Tetrault, M.D.
(for the Society of General Internal Medicine Substance Abuse Interest Group: SGIM)
Department of Internal Medicine
Yale University School of Medicine
New Haven, Connecticut

Alexander Walley, M.D., M.Sc.
(for the Society of General Internal Medicine Substance Abuse Interest Group: SGIM)
Assistant Professor of Medicine
Boston University School of Medicine, and
Medical Director, Opioid Treatment Program
Boston Public Health Commission, and
Medical Director, Opioid Overdose Prevention Program
Massachusetts Department of Public Health
Boston, Massachusetts

Norman Wetterau, M.D., FASAM
(for the Society of Teachers of Family Medicine: STFM)
University of Rochester/Highland Hospital
Tricounty Family Medicine
Nunda, New York

Regulations for the Use of Buprenorphine in Office-Based Treatment of Opioid Addiction

I. General

- Prescribers engaged in office-based opioid addiction treatment with buprenorphine shall have a waiver from the Substance Abuse Mental Health Services Administration and the appropriate Drug Enforcement Administration registration to do so.

- Prescribers shall abide by all federal and state laws and regulations governing the prescribing of buprenorphine for the treatment of opioid addiction.

- Physician assistants and nurse practitioners shall only prescribe buprenorphine for opioid addiction pursuant to a practice agreement with a waivered physician.

- Practitioners engaged in medication-assisted treatment shall provide counseling or refer the patient for counseling and document such in the medical record.

II. Patient Assessment and Treatment Planning

- A practitioner shall perform and document an assessment that includes a comprehensive medical and psychiatric history, substance abuse history, family history and psychosocial supports, appropriate physical examination, urine drug screen, pregnancy test for women of childbearing age, infectious disease testing for HIV, Hepatitis B, Hepatitis C and TB, and a check of the Prescription Monitoring Program.

- The treatment plan shall include the practitioner's rationale for selecting buprenorphine treatment, the rationale for use of the buprenorphine mono-product rather than buprenorphine/naloxone, patient education, written informed consent, how counseling will be accomplished, and a signed treatment agreement that outlines the responsibilities of the patient and the prescriber.

III. Treatment

- Buprenorphine shall not be given with other opioids, benzodiazepines , sedative hypnotics, carisoprodol, and tramadol due to a higher risk of fatal overdose, unless extenuating circumstances are documented in the medical record.

- Prior to starting medication-assisted treatment, the practitioner shall perform a check of the Prescription Monitoring Program.

- During the induction phase, the patient shall be seen 1-3 times per week.

- During the stabilization phase, increments shall be made with 2 mg. of buprenorphine per day to find the lowest dose that avoids intoxication, withdrawal, or significant drug craving.

- Practitioners shall take steps to reduce the chances of buprenorphine diversion by using the lowest effective dose, appropriate frequency of office visits, urine drug screens, pill counts and checks of the PMP.

- Documentation of the rationale for doses exceeding 16 mg. of buprenorphine per day shall be placed in the patient record.

- Behaviors that are inconsistent with the Treatment Agreement shall be discussed with the patient and documented, as well as revisions to the Treatment Agreement.

- The practitioner shall incorporate relapse prevention strategies into counseling or assure that they are addressed by a mental health professional.

- The practitioner shall document the rationale for continued medication-assisted treatment, especially beyond 2 years.

IV. Special Populations

- Pregnant and breastfeeding women shall be treated with the mono-product, usually 8 mg. per day or less, and shall not be prescribed benzodiazepines except in special circumstances that are well-documented.

- Adolescents less than 16 years shall not be prescribed buprenorphine for addiction treatment.

- The progress of patients with chronic pain shall be assessed by reduction of pain and functional objectives which can be identified, quantified and independently verified.

- Practitioners shall evaluate patients with medical comorbidities by history, physical exam, appropriate laboratory studies, and be aware of interactions of buprenorphine with other prescribed medications.

- Practitioners shall not undertake buprenorphine treatment with a patient who has psychiatric comorbidities and is not stable. The patient should be referred for psychiatric evaluation and treatment prior to initiating medication-assisted treatment.

- Recently released patients shall be assessed by the medical history, subjective report, the risk of diversion and overdose, the ability of the physician and treatment to have an impact, and other considerations.

V. Medical Records

- Records shall be timely, accurate, legible and complete.
- The treatment agreement and informed consent shall be maintained in the medical record.
- Confidentiality requirements of 42 CFR, Part 2 which prohibits release of records, re-disclosure or other information without the patient's consent or a valid court order, or in cases of a bona fide medical emergency, or in the mandatory reporting of child abuse, shall be followed.
- Compliance with Board of Medicine Regulation 18VAC85-20-27, which prohibits willful or negligent breach of confidentiality or unauthorized disclosure of confidential PMP information, shall be maintained.

12VAC30-130-5121. Covered services: Clinic services (OBOT).

A. Office-based opioid treatment (OBOT) shall be provided by a buprenorphine-waivered practitioner and may be provided in a variety of practice settings including primary care clinics, outpatient health system clinics, psychiatry clinics, Federally-Qualified Health Centers (FQHCs), Community Service Boards/BHAs, local health department clinics, and physicians' offices. The practitioner shall be contracted by the BHSA or MCO to perform OBOT services. OBOT services shall meet the following criteria.

1. OBOT service components.

a. Access to emergency medical and psychiatric care.

b. Affiliations with more intensive levels of care such as intensive outpatient programs and partial hospitalization programs that unstable individuals can be referred to when clinically indicated.

c. Individualized, patient-centered assessment and treatment.

d. Assessing, ordering, administering, reassessing, and regulating medication and dose levels appropriate to the individual; supervising withdrawal management from opioid analgesics; overseeing and facilitating access to appropriate treatment for opioid use disorder and alcohol use disorder.

e. Medication for other physical and mental illnesses shall be provided as needed either on-site or through collaboration with other providers.

f. Cognitive, behavioral, and other substance use disorder-focused therapies, reflecting a variety of treatment approaches, shall be provided to the individual on an individual, group, or family basis and shall be provided by credentialed addiction treatment professionals working in collaboration with the buprenorphine-waivered practitioner who is prescribing buprenorphine

products or naltrexone products to individuals with moderate to severe opioid use disorder. These therapies can be provided via telehealth as long as they meet the Department's requirements for an OBOT and for the use of telehealth.

g. Substance use care coordination provided including interdisciplinary care planning between buprenorphine-waivered physician and the licensed behavioral health provider to develop and monitor individualized and personalized treatment plans focused on the best outcomes for the individual. This care coordination includes monitoring individual progress, tracking individual outcomes, linking individual with community resources to facilitate referrals and respond to social service needs, and tracking and supporting the individual's medical, behavioral health, or social services received outside the practice.

h. Referral for screening for infectious diseases such as HIV, hepatitis B and C, and tuberculosis at treatment initiation and then at least annually or more often based on risk factors.

B. OBOT staff requirements.

1. Buprenorphine-waivered practitioner licensed under Virginia law who has completed one of the continuing medical education courses approved by the Center for Substance Abuse Treatment and obtained the waiver to prescribe or dispense buprenorphine for opioid use disorder required under the Drug Addiction Treatment Act of 2000 (DATA 2000). The practitioner must have a DEA-X number issued by the Drug Enforcement Agency that is included on all buprenorphine prescriptions for treatment of opioid use disorder.

2. Credentialed addiction treatment professionals shall work in collaboration with the buprenorphine-waivered practitioner who is prescribing buprenorphine products or naltrexone products to individuals with moderate to severe opioid use disorder. This collaboration can be

in-person or via telemedicine as long as it meets the department's requirements for the OBOT setting and for telehealth.

C. OBOT risk management shall include and shall be documented in each individual's record:

1. Random urine drug screening for all individuals, conducted at a minimum of eight times per year.

2. The Virginia Prescription Monitoring Program shall be checked at least quarterly for all individuals.

3. Opioid overdose prevention education including the prescribing of naloxone.

ARTS
Addiction and Recovery Treatment Services

Virginia Department of Medical Assistance Services

REQUIREMENTS FOR OFFICE-BASED OPIOID TREATMENT (OBOT) PROVIDERS

OFFICE-BASED OPIOID TREATMENT (OBOT) PROVIDERS

SETTING

Buprenorphine-waivered practitioner (physician, nurse practitioner, or physician's assistant) may practice in a variety of practice settings including primary care clinics, outpatient health system clinics, psychiatry clinics, Federally-Qualified Health Centers, Community Service Boards, Local Health Departments, and physician's offices.

SUPPORT SYSTEMS

- ☐ Access to emergency medical and psychiatric care.
- ☐ Affiliations with more intensive levels of care such as Intensive Outpatient Programs and Partial Hospitalization Programs that unstable patients can be referred to when clinically indicated.

STAFF REQUIREMENTS

- ☐ Licensed physician must have completed the 8 hour training course approved by the Substance Abuse and Mental Health Services Administration and obtained a waiver to prescribe buprenorphine for opioid use disorder from the Drug Enforcement Agency.
- ☐ Licensed NP or PA must have completed the the 24 hours of training required by the Substance Abuse and Mental Health Services Administration and obtained a waiver to prescribe buprenorphine for opioid use disorder from the Drug Enforcement Agency. NP must have collaborative practice agreement with a bupernenorphine-waivered physician. PA must be supervised by a buprenorphine-waivered physician.
- ☐ Licensed behavioral health provider (licensed psychiatrist, licensed clinical psychologist, licensed clinical social worker, licensed professional counselor, licensed psychiatric clinical nurse specialist, licensed psychiatric nurse practitioner, licensed marriage and family therapist, licensed substance abuse treatment practitioner, or Certified Substance Abuse Counselor under supervision of a licensed provider) must be co-located on-site and provide counseling during clinic sessions when the buprenorphine-waivered practitioner is prescribing buprenorphine or naltrexone to patients with opioid use disorder.[i] Counseling can be provided via telemedicine.
- ☐ Pharmacist can serve as an optional but important member of the interprofessional team. Pharmacists can advise the buprenorphine-waivered practitioner on the selection of buprenorphine vs injectible naltrexone (Vivitrol) as treatment options, assist with buprenorphine induction and dose adjustments, contribute to the development of treatment plan, and assist with monitoring and communicating with patients.
- ☐ Licensed behavioral health provider can be employed by or have a contractual relationship with the buprenorphine-waivered practitioner or the organization employing the practitioner.
- ☐ All billing by the behavioral health provider needs to be under the tax ID number of the buprenorphine-waivered practitioner or the organization employing the practitioner.

THERAPIES

- ☐ Individualized, patient-centered assessment and treatment.
- ☐ Assessing, ordering, administering, reassessing, and regulating medication and dose levels appropriate to the individual; supervising withdrawal management from opioid analgesics; overseeing and facilitating access to appropriate treatment for opioid use disorder and alcohol use disorder.
- ☐ Buprenorphine monoproduct prescribed only to pregnant women. All other patients receive buprenorphine/naloxone or naltrexone products.
- ☐ Maximum daily buprenorphine/naloxone dose of 16 mg unless there is documentation of an ongoing compelling clinical rationale for a higher maintenance dose up to maximum of 24 mg.
- ☐ No tolerance to other opioids, soma, stimulants, or benzodiazepines except for patients already on benzodiazepines for 3 months during a relapse or tapering plan.

ARTS
Addiction and Recovery Treatment Services

Virginia Department of Medical Assistance Services

REQUIREMENTS FOR OFFICE-BASED OPIOID TREATMENT (OBOT) PROVIDERS

☐ Medication for other physical and mental health disorders is provided as needed either on-site or through collaboration with other providers.

☐ Cognitive, behavioral, and other substance use disorder-focused therapies, reflecting a variety of treatment approaches, provided to the patient on an individual, group, or family basis.

☐ Care coordination provided including interdisciplinary care planning between buprenorphine-waivered practitioner and the licensed behavioral health provider to develop and monitor individualized and personalized treatment plans that are focused on the best outcomes for the patient, monitoring patient progress and tracking patient outcomes, linking patients with community resources (including Alcoholics Anonymous, Narcotics Anonymous, peer recovery supports, etc.) to facilitate referrals and respond to social service needs, and tracking and supporting patients when they obtain medical, behavioral health, or social services outside the practice.

☐ Referral for screening for HIV, Hepatitis B and C, and Tuberculosis at treatment initiation and then annually.

RISK MANAGEMENT AND ADHERENCE MONITORING

☐ Random urine drug screening, conducted a minimum of 8 times per year for all patients.

☐ Virginia Prescription Monitoring Program checked at least quarterly for all patients.

☐ Opioid overdose prevention education including the prescribing of naloxone.

☐ Patients seen at least weekly when initiating treatment. Patient must have been seen for at least 3 months with documented clinical stability before spacing out to a minimum of monthly visits with buprenorphine-waivered practitioner or licensed behavioral health provider.

☐ Periodic utilization of unused medication and opened medication wrapper counts when clinically indicated.

---

[i] Community Service Boards and Federally-Qualified Health Centers are not required to have the licensed behavioral health provider co-located on-site and providing counseling during clinic sessions when the buprenorphine-waivered practitioner is prescribing buprenorphine or naltrexone to patients with opioid use disorder. The licensed behavioral health provider must be employed by the same organization and providing counseling to patients prescribed buprenorphine or naltrexone. They must engage in interdisciplinary care planning with the buprenorphine-waivered practitioner including working together to develop and monitor individualized and personalized treatment plans that are focused on the best outcomes for the patient.

Guidance document: 85-24 Revised: October 24, 2013

Virginia Board of Medicine

Guidance on the Use of Opioid Analgesics in the Treatment of Chronic Pain

In 2004, the Virginia Board of Medicine adopted the Federation of State Medical Boards' Model Policy on the Use of Controlled Substances in the Treatment of Pain as Board Guidance Document 85-24. It served as a guide to licensees who accepted the challenge of treating chronic pain, informed the Board members of the essential aspects of good pain management, and also provided the public with perspective on this sometimes controversial field of medicine.

As the thinking about chronic pain management has evolved, the Federation of State Medical Boards revisited the issue in 2012-2013 and produced a subsequent version of the Model Policy. At its October 24, 2013 meeting, the Board voted to replace the 2004 version with the 2013 Model Policy for the Use of Opioid Analgesics in the Treatment of Chronic Pain[i] to serve as its guidance in this matter.

[i] Reprinted with permission of the Federation of State Medical Boards, October 25, 2013

STATE MEDICAL BOARDS

Model Policy on the Use of Opioid Analgesics in the Treatment of Chronic Pain

July 2013

The recommendations contained herein were adopted as policy by the Executive Committee of the Federation of State Medical Boards of the United States, Inc., July 2013.

(817) 868-4000 | www.fsmb.org

Federation of STATE MEDICAL BOARDS

MODEL POLICY ON THE USE OF OPIOID ANALGESICS IN THE TREATMENT OF CHRONIC PAIN

INTRODUCTION

The Federation of State Medical Boards (FSMB) is committed to assisting state Medical Boards in protecting the public and improving the quality and integrity of health care in the United States. In 1997, the FSMB undertook an initiative to develop model guidelines and to encourage state medical boards and other health care regulatory agencies to adopt policies encouraging safe and effective treatment of patients with pain, including, if indicated, the use of opioid analgesics. [1]. The FSMB updated its guidelines in 2003 [2] so that its Model Policy would reflect the best available evidence on management of pain and give adequate attention to both the undertreatment and overtreatment of pain and the inappropriate use of opioid analgesics.

Through these initiatives, the FSMB has sought to provide a resource for use by state medical boards in educating their licensees about cautious and responsible prescribing of controlled substances while alleviating fears of regulatory scrutiny. The FSMB recognizes that inappropriate prescribing can contribute to adverse outcomes such as reduced function, opioid addiction, overdose, and death [3-5]. By promulgating its Model Policies, the FSMB has sought to provide a framework for the legitimate medical use of opioid analgesics for the treatment of pain while emphasizing the need to safeguard against their misuse and diversion.

Since their publication, the 1998 and 2004 Model Policies have been widely distributed to state medical boards, medical professional organizations, other health care regulatory boards, patient advocacy groups, pharmaceutical companies, state and federal regulatory agencies, and practicing physicians and other health care providers. The policies have been endorsed by the American Academy of Pain Medicine, the Drug Enforcement Administration, the American Pain Society, and the National Association of State Controlled Substances Authorities. Many states have adopted all or part of the Model Policies.[1]

The updated Model Policy presented here reflects the considerable body of research and experience accrued since the 2004 revision was adopted [2]. While recognizing that adequate evidence is currently lacking as to the effectiveness and safety of long-term opioid therapy, this Model Policy is designed to promote the public health by encouraging state medical boards to adopt consistent policy regarding the treatment of pain, particularly chronic pain, and to promote patient access to appropriate pain management and, if indicated, substance abuse and addiction treatment. The Model Policy emphasizes the professional and ethical responsibility of physicians to appropriately assess and manage patients' pain, assess the relative level of risk for misuse and addiction, monitor for aberrant behaviors and intervene as appropriate. It also includes references and the definitions of key terms used in pain management.

[1] As of March 7, 2012, 57 of 70 State Medical Boards have policy, rules, regulations or statutes reflecting the Federation's 1997 or 2004 *Model Guidelines for the Use of Controlled Substances for the Treatment of Pain.*

The FSMB encourages every state medical board to work with the state attorney general to evaluate the state's policies, regulations and laws in an effort to identify any barriers to the effective and appropriate use of opioids to relieve pain, while ensuring that adequate safeguards are in place to deter and rapidly detect those who would obtain opioid analgesics for nonmedical purposes [6-7].

The FSMB acknowledges with gratitude the efforts of the stare board members and directors who collaborated to prepare this updared Model Policy, as well as the contributions of the independent experts and medical organizations that advised the drafting committee and reviewed its work. The FSMB also thanks SAMHSA for its support of this important project.

ISSUES ADDRESSED IN THE NEW MODEL POLICY

There is a significant body of evidence suggesting that many Americans suffer from chronic pain and much of that pain is inadequately or ineffectively treared[8-10]. Since the 2004 revision, evidence for risk associated with opioids has snrged, while evidence for benefits has remained controversial and insufficient. Over the last decade, there has been a parallel increase in opioid sales and an increase in morbidity and mortality associated with these drugs. At the same time, approximately one in four patients seen in primary care settings suffers from pain so intense as to interfere with the activities of daily living [4]. Pain arises from multiple causes and often is categorized as either *acute pain* (such as that from traumatic injury and surgery) or *chronic pain* (such as the pain associated with terminal conditions such as cancer or severe vascular disease or with non-terminal conditions such as arthritis or neuropathy) [4,8]. This model policy applies most directly ro the treatment of chronic pain and the use of opioid analgesics but many of the strategies to improve appropriate prescribing and mitigate risks can be applied to the use of other controlled medications and ro the treatment of acute pain.

Undertreatment of pain is recognized as a serious public health problem that compromises patients' functional status and quality of life [4,9]. A myriad of psychological, social, economic, political, legal and educational factors—including inconsistencies and restrictions in state pain policies—can either facilitate or impede the ability and willingness of physicians to manage patients with pain [6,10-11].

While acknowledging that undertreatment of pain exists, it must be understood that chronic pain often is intractable, that the current state of medical knowledge and medical therapies, including opioid analgesics, does not provide for complete elimination of chronic pain in most cases, and that the existence of persistent and disabling pain does not in and of itself constitute evidence of undertreatment [4,8,12]. Indeed, some cases of intractable pain actually result from overtreatment in terms of procedures and medications.

Complicating the picture, adverse outcomes associated with the misuse, abuse and diversion of prescription opioids have increased dramatically since the FSMB's last review [3]. Physicians and other health care professionals have contributed—often inadvertently—to these increases.

Circumstances that contribute to both the inadequate treatment of pain and the inappropriate prescribing of opioids by physicians may include: (1) physician uncertainty or lack of knowledge as to prevailing best clinical practices; (2) inadequate research into the sources of and treatments for pain; (3) sometimes conflicting clinical guidelines for appropriate treatment of pain; (4) physician concerns that prescribing needed amounts of opioid analgesics will result in added scrutiny by regulatory authorities; (5) physician misunderstanding of causes and manifestations of opioid dependence and addiction; (6) fear on the part of physicians of causing addiction or being deceived by a patient who seeks drugs for purposes of misuse; (7) physicians practicing outside the bounds

of professional conduct by prescribing opioid analgesics without a legitimate medical purpose; and (8) inadequate physician education about regulatory policies and processes [3-4,12,14-20]. Inappropriate treatment also can result from a mistaken belief on the part of patients and their physicians that complete eradication of pain is an attainable goal, and one that can be achieved without disabling adverse effects. Additionally, treatment options may be limited based on availability and/or health plan policies on covered benefits or drug formularies.

Patients share with physicians a responsibility for appropriate use of opioid analgesics [21-22]. This responsibility encompasses providing the physician with complete and accurate information and adhering to the treatment plan. While many patients take their medication safely as prescribed and do not use opioids problematically, some patients—intentionally or unintentionally—are less than forthcoming or have unrealistic expectations regarding the need for opioid therapy or the amount of medication required. Other patients may begin to use medications as prescribed, then slowly deviate from the therapeutic regimen. Still others may not comply with the treatment plan because they misunderstood the physician's instructions. Some patients share their drugs with others without intending harm (a pattern of misuse that is seen quite often among older adults [15]). Then there are patients who deliberately misuse or are addicted to opioids, and who mislead, deceive or fail to disclose information to their physicians in order to obtain opioids to sustain their addiction and avoid withdrawal [19-23].

Patients often leave medications unsecured where they can be stolen by visitors, workers and family members, which is another important source of diversion. Thus a prescription that is quite appropriate for an elderly patient may ultimately contribute to the death of a young person who visits or lives in the patient's home. Therefore, the physician's duty includes not only appropriate prescribing of opioid analgesics, but also appropriate education of patients regarding the secure storage of medications and their appropriate disposal once the course of treatment is completed [18,23].

A more problematic individual is the criminal patient, whose primary purpose is to obtain drugs for resale. Whereas many addicted patients seek a long-term relationship with a prescriber, criminal patients sometimes move rapidly from one prescriber (or dispenser) to another. Such individuals often visit multiple practitioners (a practice sometimes characterized as "doctor shopping") and travel from one geographic area to another not for the purposes of relief of legitimate pain but in search of unsuspecting targets [19-21]. Physicians' attention to patient assessment and the routine use of state prescription drug monitoring programs (PDMPs), where available, have been cited as effective ways to identify individuals who engage in such criminal activities [20-23,45].

Conclusion: The goal of this Model Policy is to provide state medical boards with an updated guideline for assessing physicians' management of pain, so as to determine whether opioid analgesics are used in a manner that is both medically appropriate and in compliance with applicable state and federal laws and regulations. The revised Model Policy makes it clear that the state medical board will consider inappropriate management of pain, particularly chronic pain, to be a departure from accepted best clinical practices, including, but not limited to the following:

- **Inadequate attention to initial assessment to determine if opioids are clinically indicated and to determine risks associated with their use in a particular individual with pain:** Not unlike many drugs used in medicine today, there are significant risks associated with opioids and therefore benefits must outweigh the risks.

- **Inadequate monitoring during the use of potentially abusable medications:** Opioids may be associated with addiction, drug abuse, aberrant behaviors, chemical coping and other dysfunctional

behavioral problems, and some patients may benefit from opioid dose reductions or tapering or weaning off the opioid.

- **Inadequate attention to patient education and informed consent:** The decision to begin opioid therapy for chronic pain should be a shared decision of the physician and patient after a discussion of the risks and a clear understanding that the clinical basis for the use of these medications for chronic pain is limited, that some pain may worsen with opioids, and taking opioids with other substances or certain condition (i.e. sleep apnea, mental illness, pre-existing substance use disorder) may increase risk.

- **Unjustified dose escalation without adequate attention to risks or alternative treatments:** Risks associated with opioids increase with escalating doses as well as in the setting of other comorbidities (i.e. mental illness, respiratory disorders, pre-existing substance use disorder and sleep apnea) and with concurrent use with respiratory depressants such as benzodiazepines or alcohol.

- **Excessive reliance on opioids, particularly high dose opioids for chronic pain management:** Prescribers should be prepared for risk management with opioids in advance of prescribing and should use opioid therapy for chronic non-cancer pain only when safer and reasonably effective options have failed. Maintain opioid dosage as low as possible and continue only if clear and objective outcomes are being met.

- **Not making use of available tools for risk mitigations:** When available, the state prescription drug monitoring program should be checked in advance of prescribing opioids and should be available for ongoing monitoring.

In addition, the Model Policy is designed to communicate to licensees that the state medical board views pain management as an important area of patient care that is integral to the practice of medicine; that opioid analgesics may be necessary for the relief of certain pain conditions; and that physicians will not be sanctioned solely for prescribing opioid analgesics or the dose (mg./mcg.) prescribed for legitimate medical purposes. However, prescribers must be held to a safe and best clinical practice. The federal Controlled Substances Act [25] defines a "lawful prescription" as one that is issued for a legitimate medical purpose by a practitioner acting in the usual course of professional practice. The use of opioids for other than legitimate medical purposes poses a threat to the individual and to the public health, thus imposing on physicians a responsibility to minimize the potential for misuse, abuse and diversion of opioids and all other controlled substances.

MODEL POLICY FOR THE USE OF OPIOID ANALGESICS IN THE TREATMENT OF CHRONIC PAIN

SECTION I: PREAMBLE

The (name of Board) is obligated under the laws of the State of (name of state) to protect the public health and safety. The (name of Board) recognizes that principles of high-quality medical practice dictate that the people of the State of (name of state) have access to appropriate, safe and effective pain management. The application of up-to-date knowledge and treatment modalities can help to restore function and thus improve the quality of life of patients who suffer from pain, particularly chronic pain [4,8,26].

This policy has been developed to articulate the Board's position on the use of controlled substances for pain, particularly the use of opioid analgesics and with special attention to the management of chronic pain. The policy thus is intended to encourage physicians to be knowledgeable about best clinical practices as regards the prescribing of opioids and be aware of associated risks. For the purposes of this policy, inappropriate treatment of pain includes non-treatment, inadequate treatment, overtreatment, and continued use of ineffective treatments.

The Board recognizes that opioid analgesics are useful and can be essential in the treatment of acute pain that results from trauma or surgery, as well as in the management of certain types of chronic pain, whether due to cancer or non-cancer causes [20,26,28]. The Board will refer to current clinical practice guidelines and expert reviews in approaching allegations of possible mismanagement of pain [8,10,12,14,26-41, 80].

Responsibility for Appropriate Pain Management: All physicians and other providers should be knowledgeable about assessing patients' pain and function, and familiar with methods of managing pain [4,16]. Physicians also need to understand and comply with federal and state requirements for prescribing opioid analgesics [3,12,19]. Whenever federal laws and regulations differ from those of a particular state, the more stringent rule is the one that should be followed [42].

Physicians should not fear disciplinary action from the Board for ordering, prescribing, dispensing or administering controlled substances, including opioid analgesics, for a legitimate medical purpose and in the course of professional practice, when current best clinical practices are met.

The Board will consider the use of opioids for pain management to be for a legitimate medical purpose if it is based on sound clinical judgment and current best clinical practices, is appropriately documented, and is of demonstrable benefit to the patient. To be within the usual course of professional practice, a legitimate physician-patient relationship must exist and the prescribing or administration of medications should be appropriate to the identified diagnosis, should be accompanied by careful follow-up monitoring of the patient's response to treatment as well as his or her safe use of the prescribed medication, and should demonstrate that the therapy has been adjusted as needed [7,38,43]. There should be documentation of appropriate referrals as necessary [36-37].

The medical management of pain should reflect current knowledge of evidence-based or best clinical practices for the use of pharmacologic and nonpharmacologic modalities, including the use of opioid analgesics and non-opioid therapies [14,16,27]. Such prescribing must be based on careful assessment of the patient and his or her pain (see the discussion on risk stratification, below) [33].

Pain should be assessed and treated promptly, and the selection of therapeutic modalities (including the quantity and frequency of medication doses) should be adjusted according to the nature of the pain, the patient's response to treatment, and the patient's risk level relative to the use of medications with abuse potential [8,10,12,14,26-38].

Preventing Opioid Diversion and Abuse: The Board also recognizes that individuals' use of opioid analgesics for other than legitimate medical purposes poses a significant threat to the health and safety of the individual as well as to the public health [3]. The Board further recognizes that inappropriate prescribing of controlled substances by physicians may contribute to drug misuse and diversion by individuals who seek opioids for other than legitimate medical purposes [5,19,44]. Accordingly, the Board expects physicians to incorporate safeguards into their practices to minimize the risk of misuse and diversion of opioid analgesics and other controlled substances [19-23,38,45-46].

Allegations of inappropriate pain management will be evaluated on an individual basis. The Board may use a variety of sources to determine the appropriateness of treatment including prescribing information obtained from the State Prescription Drug Monitoring Program. The Board will not take disciplinary action against a physician for deviating from this Model Policy when contemporaneous medical records show reasonable cause for such a deviation.

The Board will judge the validity of the physician's treatment of a patient on the basis of available documentation, rather than solely on the quantity and duration of medication administered. The goal is the management of the patient's pain while effectively addressing other aspects of the patient's functioning, including physical, psychological, social and work-related factors, and mitigating risk of misuse, abuse, diversion and overdose [4,29].

The Board will consider the unsafe or otherwise inappropriate treatment of pain to be a departure from best clinical practice, taking into account whether the treatment is appropriate to the diagnosis and the patient's level of risk.

SECTION II: GUIDELINES

The Board has adopted the following criteria for use in evaluating a physician's management of a patient with pain, including the physician's prescribing of opioid analgesics:

Understanding Pain: The diagnosis and treatment of pain is integral to the practice of medicine [4,34-37]. In order to cautiously prescribe opioids, physicians must understand the relevant pharmacologic and clinical issues in the use of such analgesics, and carefully structure a treatment plan that reflects the particular benefits and risks of opioid use for each individual patient. Such an approach should be employed in the care of every patient who receives chronic opioid therapy [4,8].

Patient Evaluation and Risk Stratification: The medical record should document the presence of one or more recognized medical indications for prescribing an opioid analgesic [7] and reflect an appropriately detailed patient evaluation [38]. Such an evaluation should be completed before a decision is made as to whether to prescribe an opioid analgesic.

The nature and extent of the evaluation depends on the type of pain and the context in which it occurs. For

example, meaningful assessment of chronic pain, including pain related to cancer or non-cancer origins, usually demands a more detailed evaluation than an assessment of acute pain. Assessment of the patient's pain typically would include the nature and intensity of the pain, past and current treatments for the pain, any underlying or co-occurring disorders and conditions, and the effect of the pain on the patient's physical and psychological functioning [31].

For every patient, the initial work-up should include a systems review and relevant physical examination, as well as laboratory investigations as indicated [33,36,48-53]. Such investigations help the physician address not only the nature and intensity of the pain, but also its secondary manifestations, such as its effects on the patient's sleep, mood, work, relationships, valued recreational activities, and alcohol and drug use.

Social and vocational assessment is useful in identifying supports and obstacles to treatment and rehabilitation; for example: Does the patient have good social supports, housing, and meaningful work? Is the home environment stressful or nurturing? [14].

Assessment of the patient's personal and family history of alcohol or drug abuse and relative risk for medication misuse or abuse also should be part of the initial evaluation [11,14,21-23,45], and ideally should be completed prior to a decision as to whether to prescribe opioid analgesics [56-58]. This can be done through a careful clinical interview, which also should inquire into any history of physical, emotional or sexual abuse, because those are risk factors for substance misuse [31]. Use of a validated screening tool (such as the Screener and Opioid Assessment for Patients with Pain [SOAPP-R; 48] or the Opioid Risk Tool [ORT; 49]), or other validated screening tools, can save time in collecting and evaluating the information and determining the patient's level of risk.

All patients should be screened for depression and other mental health disorders, as part of risk evaluation. Patients with untreated depression and other mental health problems are at increased risk for misuse or abuse of controlled medications, including addiction, as well as overdose.

Patients who have a history of substance use disorder (including alcohol) are at elevated risk for failure of opioid analgesic therapy to achieve the goals of improved comfort and function, and also are at high risk for experiencing harm from this therapy, since exposure to addictive substances often is a powerful trigger of relapse [11,31,45]. Therefore, treatment of a patient who has a history of substance use disorder should, if possible, involve consultation with an addiction specialist before opioid therapy is initiated (and follow-up as needed). Patients who have an active substance use disorder should not receive opioid therapy until they are established in a treatment/recovery program [31] or alternatives are established such as co-management with an addiction professional. Physicians who treat patients with chronic pain should be encouraged to also be knowledgeable about the treatment of addiction, including the role of replacement agonists such as methadone and buprenorphine. For some physicians, there may be advantages to becoming eligible to treat addiction using office-based buprenorphine treatment.

Information provided by the patient is a necessary but insufficient part of the evaluation process. Reports of previous evaluations and treatments should be confirmed by obtaining records from other providers, if possible. Patients have occasionally provided fraudulent records, so if there is any reason to question the truthfulness of a patient's report, it is best to request records directly from the other providers [54-55].

If possible, the patient evaluation should include information from family members and/or significant others [22-23,49-50]. Where available, the state prescription drug monitoring program (PDMP) should be consulted

to determine whether the patient is receiving prescriptions from any other physicians, and the results obtained from the PDMP should be documented in the patient record [34].

In dealing with a patient who is taking opioids prescribed by another physician—particularly a patient on high doses—the evaluation and risk stratification assume even greater importance [21-23]. With all patients, the physician's decision as to whether to prescribe opioid analgesics should reflect the totality of the information collected, as well as the physician's own knowledge and comfort level in prescribing such medications and the resources for patient support that are available in the community [21-23].

Development of a Treatment Plan and Goals: The goals of pain treatment include reasonably attainable improvement in pain and function; improvement in pain-associated symptoms such as sleep disturbance, depression, and anxiety; and avoidance of unnecessary or excessive use of medications [4,8]. Effective means of achieving these goals vary widely, depending on the type and causes of the patient's pain, other concurrent issues, and the preferences of the physician and the patient.

The treatment plan and goals should be established as early as possible in the treatment process and revisited regularly, so as to provide clear-cut, individualized objectives to guide the choice of therapies [38]. The treatment plan should contain information supporting the selection of therapies, both pharmacologic (including medications other than opioids) and nonpharmacologic. It also should specify the objectives that will be used to evaluate treatment progress, such as relief of pain and improved physical and psychosocial function [14,36,47].

The plan should document any further diagnostic evaluations, consultations or referrals, or additional therapies that have been considered [21-23,45].

Informed Consent and Treatment Agreement: The decision to initiate opioid therapy should be a shared decision between the physician and the patient. The physician should discuss the risks and benefits of the treatment plan (including any proposed use of opioid analgesics) with the patient, with persons designated by the patient, or with the patient's surrogate or guardian if the patient is without medical decision-making capacity [32,35]. If opioids are prescribed, the patient (and possibly family members) should be counseled on safe ways to store and dispose of medications [3,37].

Use of a written informed consent and treatment agreement (sometimes referred to as a "treatment contract") is recommended [21-23,35,38].

Informed consent documents typically address:

- The potential risks and anticipated benefits of chronic opioid therapy.
- Potential side effects (both short- and long-term) of the medication, such as constipation and cognitive impairment.
- The likelihood that tolerance to and physical dependence on the medication will develop.
- The risk of drug interactions and over-sedation.
- The risk of impaired motor skills (affecting driving and other tasks).
- The risk of opioid misuse, dependence, addiction, and overdose.
- The limited evidence as to the benefit of long-term opioid therapy.
- The physician's prescribing policies and expectations, including the number and frequency of prescription refills, as well as the physician's policy on early refills and replacement of lost or stolen medications.
- Specific reasons for which drug therapy may be changed or discontinued (including violation of the policies and agreements spelled out in the treatment agreement).

Treatment agreements outline the joint responsibilities of physician and patient [35-37] and are indicated for opioid or other abusable medications. They typically discuss:

- The goals of treatment, in terms of pain management, restoration of function, and safety.
- The patient's responsibility for safe medication use (e.g., by not using more medication than prescribed or using the opioid in combination with alcohol or other substances; storing medications in a secure location; and safe disposal of any unused medication).
- The patient's responsibility to obtain his or her prescribed opioids from only one physician or practice.
- The patient's agreement to periodic drug testing (as of blood, urine, hair, or saliva).
- The physician's responsibility to be available or to have a covering physician available to care for unforeseen problems and to prescribe scheduled refills.

Informed consent documents and treatment agreements can be part of one document for the sake of convenience.

Initiating an Opioid Trial: Generally, safer alternative treatments should be considered before initiating opioid therapy for chronic, non-malignant pain. Opioid therapy should be presented to the patient as a therapeutic trial or test for a defined period of time (usually no more than 90 days) and with specified evaluation points. The physician should explain that progress will be carefully monitored for both benefit and harm in terms of the effects of opioids on the patient's level of pain, function, and quality of life, as well as to identify any adverse events or risks to safety [51]. When initiating opioid therapy, the lowest dose possible should be given to an opioid naïve patient and titrate to affect. It is generally suggested to begin opioid therapy with a short acting opioid and rotate to a long acting/extended release if indicated.

A decision to continue opioid therapy beyond the trial period should reflect a careful evaluation of benefits versus adverse events [29]and/or potential risks.

Ongoing Monitoring and Adapting the Treatment Plan: The physician should regularly review the patient's progress, including any new information about the etiology of the pain or the patient's overall health and level of function [35,49-50]. When possible, collateral information about the patient's response to opioid therapy should be obtained from family members or other close contacts, and the state PDMP. The patient should be seen more frequently while the treatment plan is being initiated and the opioid dose adjusted [44-51]. As the patient is stabilized in the treatment regimen, follow-up visits may be scheduled less frequently. (However, if the patient is seen less than monthly and an opioid is prescribed, arrangements must be made for the patient to obtain a refill or new prescription when needed.)

At each visit, the results of chronic opioid therapy should be monitored by assessing what have been called the "5As" of chronic pain management; these involve a determination of whether the patient is experiencing a reduction in pain (Analgesia), has demonstrated an improvement in level of function (Activity), whether there are significant Adverse effects, whether there is evidence of Aberrant substance-related behaviors, and mood of the individual (Affect) [38,52]. Validated brief assessment tools that measure pain and function, such as the three-question "Pain, Enjoyment and General Activity" (PEG) scale [47] or other validated assessment tools, may be helpful and time effective.

Continuation, modification or termination of opioid therapy for pain should be contingent on the physician's evaluation of (1) evidence of the patient's progress toward treatment objectives and (2) the absence of substantial

risks or adverse events, such as overdose or diversion [21-23,45]. A satisfactory response to treatment would be indicated by a reduced level of pain, increased level of function, and/or improved quality of life [29]. Information from family members or other caregivers should be considered in evaluating the patient's response to treatment [14,35-36]. Use of measurement tools to assess the patient's level of pain, function, and quality of life (such as a visual analog or numerical scale) can be helpful in documenting therapeutic outcomes [14,49].

Periodic Drug Testing: Periodic drug testing may be useful in monitoring adherence to the treatment plan, as well as in detecting the use of non-prescribed drugs [53-54]. Drug testing is an important monitoring tool because self-reports of medication use is not always reliable and behavioral observations may detect some problems but not others [55-59]. Patients being treated for addiction should be tested as frequently as necessary to ensure therapeutic adherence, but for patients being treated for pain, clinical judgment trumps recommendations for frequency of testing.

Urine may be the preferred biologic specimen for testing because of its ease of collection and storage and the cost-effectiveness of such testing [53]. When such testing is conducted as part of pain treatment, forensic standards are generally not necessary and not in place, so collection is not observed and chain-of-custody protocols are not followed. Initial testing may be done using class-specific immunoassay drug panels (point-of-care or laboratory-based), which typically do not identify particular drugs within a class unless the immunoassay is specific for that drug. If necessary, this can be followed up with a more specific technique, such as gas chromotography/mass spectrometry (GC/MS) or other chromatographic tests to confirm the presence or absence of a specific drug or its metabolites [53]. In drug testing in a pain practice, it is important to identify the specific drug not just the class of the drug.

Physicians need to be aware of the limitations of available tests (such as their limited sensitivity for many opioids) and take care to order tests appropriately [54]. For example, when a drug test is ordered, it is important to specify that it include the opioid being prescribed [53]. Because of the complexities involved in interpreting drug test results, it is advisable to confirm significant or unexpected results with the laboratory toxicologist or a clinical pathologist [59-60].

While immunoassay, point of care (POC) testing has its utility in the making of temporary and "on the spot" changes in clinical management, its limitations with regard to accuracy have recently been the subject of study. These limitations are such that the use of point of care testing for the making of more long term and permanent changes in management of people with the disease of addiction and other clinical situations may not be justified until the results of confirmatory testing with more accurate methods such as LC-MS/MS are obtained. A recent study on LC-MS/MS results following immunoassay POC testing in addiction treatment settings and found very high rates of "false negatives and positives" [53,81].

Test results that suggest opioid misuse should be discussed with the patient. It is helpful to approach such a discussion in a positive, supportive fashion, so as to strengthen the physician-patient relationship and encourage healthy behaviors (as well as behavioral change where that is needed). Both the test results and subsequent discussion with the patient should be documented in the medical record [53].

Periodic pill counting is also a useful strategy to confirm medication adherence and to minimize diversion (e.g., selling, sharing or giving away medications). As noted earlier and where available, consulting the state's PDMP before prescribing opioids for pain and during ongoing use is highly recommended. A PDMP can be useful in monitoring compliance with the treatment agreement as well as identifying individuals obtaining controlled substances from multiple prescribers [21-23,55,62].

If the patient's progress is unsatisfactory, the physician must decide whether to revise or augment the treatment plan, whether other treatment modalities should be added to or substituted for the opioid therapy, or whether a different approach—possibly involving referral to a pain specialist or other health professional—should be employed [35-37,62-63].

Evidence of misuse of prescribed opioids demands prompt intervention by the physician [19,21-23,32,35]. Patient behaviors that require such intervention typically involve recurrent early requests for refills, multiple reports of lost or stolen prescriptions, obtaining controlled medications from multiple sources without the physician's knowledge, intoxication or impairment (either observed or reported), and pressuring or threatening behaviors [23]. The presence of illicit or unprescribed drugs, (drugs not prescribed by a physician) in drug tests similarly requires action on the part of the prescriber. Some aberrant behaviors are more closely associated with medication misuse than others [62-63]. Most worrisome is a pattern of behavior that suggests recurring misuse, such as unsanctioned dose escalations, deteriorating function, and failure to comply with the treatment plan [64].

Documented drug diversion or prescription forgery, obvious impairment, and abusive or assaultive behaviors require a firm, immediate response [22-23,38,46]. Indeed, failure to respond can place the patient and others at significant risk of adverse consequences, including accidental overdose, suicide attempts, arrests and incarceration, or even death [23,65-67]. For this reason, physicians who prescribe chronic opioid therapy should be knowledgeable in the diagnosis of substance use disorders and able to distinguish such disorders from physical dependence—which is expected in chronic therapy with opioids and many sedatives.

Consultation and Referral: The treating physician should seek a consultation with, or refer the patient to, a pain, psychiatry, addiction or mental health specialist as needed [37-38]. For example, a patient who has a history of substance use disorder or a co-occurring mental health disorder may require specialized assessment and treatment, if available [31,66].

Physicians who prescribe chronic opioid therapy should be familiar with treatment options for opioid addiction (including those available in licensed opioid treatment programs [OTPs]) and those offered by an appropriately credentialed and experienced physician through office-based opioid treatment [OBOT]), so as to make appropriate referrals when needed [23,31,37,39].

Discontinuing Opioid Therapy: Throughout the course of opioid therapy, the physician and patient should regularly weigh the potential benefits and risks of continued treatment and determine whether such treatment remains appropriate [46].

If opioid therapy is continued, the treatment plan may need to be adjusted to reflect the patient's changing physical status and needs, as well as to support safe and appropriate medication use [22-23].

Reasons for discontinuing opioid therapy include resolution of the underlying painful condition, emergence of intolerable side effects, inadequate analgesic effect, failure to improve the patient's quality of life despite reasonable titration, deteriorating function, or significant aberrant medication use [38, 45].

If opioid therapy is discontinued, the patient who has become physically dependent should be provided with a safely structured tapering regimen. Withdrawal can be managed either by the prescribing physician or by referring the patient to an addiction specialist [63]. The termination of opioid therapy should not mark the end of

treatment, which should continue with other modalities, either through direct care or referral to other health care specialists, as appropriate [21-23].

Additionally, providers should not continue opioid treatment unless the patient has received a benefit, including demonstrated functional improvement.

Medical Records: Every physician who treats patients for chronic pain must maintain accurate and complete medical records. Information that should appear in the medical record includes the following [22-23,38,43-44]:

- Copies of the signed informed consent and treatment agreement.
- The patient's medical history.
- Results of the physical examination and all laboratory tests.
- Results of the risk assessment, including results of any screening instruments used.
- A description of the treatments provided, including all medications prescribed or administered (including the date, type, dose and quantity).
- Instructions to the patient, including discussions of risks and benefits with the patient and any significant others.
- Results of ongoing monitoring of patient progress (or lack of progress) in terms of pain management and functional improvement.
- Notes on evaluations by and consultations with specialists.
- Any other information used to support the initiation, continuation, revision, or termination of treatment and the steps taken in response to any aberrant medication use behaviors [21-23,30,38,45,68]. These may include actual copies of, or references to, medical records of past hospitalizations or treatments by other providers.
- Authorization for release of information to other treatment providers.

The medical record must include all prescription orders for opioid analgesics and other controlled substances, whether written or telephoned. In addition, written instructions for the use of all medications should be given to the patient and documented in the record [25]. The name, telephone number, and address of the patient's pharmacy also should be recorded to facilitate contact as needed [23]. Records should be up-to-date and maintained in an accessible manner so as to be readily available for review [25].

Good records demonstrate that a service was provided to the patient and establish that the service provided was medically necessary. Even if the outcome is less than optimal, thorough records protect the physician as well as the patient [23,38,45,68].

Compliance with Controlled Substance Laws and Regulations: To prescribe, dispense or administer controlled substances, the physician must be registered with the DEA, licensed by the state in which he or she practices, and comply with applicable federal and state regulations [25].

Physicians are referred to the *Physicians' Manual of the U.S. Drug Enforcement Administration* (and any relevant documents issued by the state medical Board) for specific rules and regulations governing the use of controlled substances. Additional resources are available on the DEA's website (at www.deadiversion.usdoj.gov), as well as from (*any relevant documents issued by the state medical board*).

SECTION III: DEFINITIONS

For the purposes of this Model Policy, the following terms are defined as shown.

Aberrant Substance Use Behaviors: Behaviors that are outside the boundaries of the agreed-upon treatment plan may constitute aberrant substance use behaviors [22-23]. For example, obtaining prescriptions for the same or similar drugs from more than one physician or other health care provider without the treating physician's knowledge is aberrant behavior, as is use of illicit drugs.

Abuse: Abuse has been described as a maladaptive pattern of drug use that results in harm or places the individual at risk of harm [29]. Abuse of a prescription medication involves its use in a manner that deviates from approved medical, legal, and social standards, generally to achieve a euphoric state ("high") or to sustain opioid dependence that is opioid addiction or that is other than the purpose for which the medication was prescribed [28].

Addiction: A longstanding definition of addiction is that it is "a primary, chronic, neurobiologic disease, whose development and manifestations are influenced by genetic, psychosocial, and environmental factors" [28]. Addiction often is said to be characterized by behaviors that include impaired control over drug use, craving, compulsive use, and continued use despite harm [28].

A newer definition, adopted by the American Society of Addiction Medicine in 2011, describes addiction as "a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors. Addiction is characterized by inability to consistently abstain, impairment in behavioral control, craving, diminished recognition of significant problems with one's behaviors and interpersonal relationships, and a dysfunctional emotional response. Like other chronic diseases, addiction often involves cycles of relapse and remission. Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death" [40].

(As discussed below, physical dependence and tolerance are expected physiological consequences of extended opioid therapy for pain and in this context do not indicate the presence of addiction.)

Controlled Substance: A controlled substance is a drug that is subject to special requirements under the federal Controlled Substances Act of 1970 (CSA) [25], which is designed to ensure both the availability and control of regulated substances. Under the CSA, availability of regulated drugs for medical purposes is accomplished through a system that establishes quotas for drug production and a distribution system that closely monitors the importation, manufacture, distribution, prescribing, dispensing, administering, and possession of controlled drugs. Civil and criminal sanctions for serious violations of the statute are part of the government's control apparatus. The Code of Federal Regulations (Title 21, Chapter 2) implements the CSA.

The CSA provides that responsibility for scheduling controlled substances is shared between the Food and Drug Administration (FDA) and the DEA. In granting regulatory authority to these agencies, the Congress noted that both public health and public safety needs are important and that neither takes primacy over the other. To accomplish this, the Congress provided guidance in the form of factors that must be considered by the FDA and DEA when assessing public health and safety issues related to a new drug or one that is being considered for rescheduling or removal from control.

The CSA does *not* limit the amount of drug prescribed, the duration for which it is prescribed, or the period for which a prescription is valid (although some states do impose such limits).

Most potent opioid analgesics are classified in *Schedules II* or *III* under the CSA, indicating that they have a significant potential for abuse and a currently accepted medical use in treatment in the U.S. (with certain restrictions), and that abuse of the drug may lead to severe psychological or physical dependence. Although the scheduling system provides a rough guide to abuse potential, it should be recognized that all controlled medications have some potential for abuse.

Dependence: Physical dependence is a state of biologic adaptation that is evidenced by a class-specific withdrawal syndrome when the drug is abruptly discontinued or the dose rapidly reduced, and/or by the administration of an antagonist [28]. It is important to distinguish addiction from the type of physical dependence that can and does occur within the context of good medical care, as when a patient on long-term opioid analgesics for pain becomes physically dependent on the analgesic. This distinction is reflected in the two primary diagnostic classification systems used by health care professionals: the *International Classification of Mental and Behavioural Disorders, 10th Edition* (ICD-10) of the World Health Organization [70], and the *Diagnostic and Statistical Manual* (*DSM*) of the American Psychiatric Association [71]. In the DSM-IV-TR, a diagnosis of "substance dependence" meant addiction. In the upcoming DSM V, the term *dependence* is reestablished in its original meaning of physiological dependence. When symptoms are sufficient to meet criteria for substance misuse or addiction, the term "substance use disorder" is used, accompanied by severity ratings [69].

It may be important to clarify this distinction during the informed consent process, so that the patient (and family) understands that physical dependence and tolerance are likely to occur if opioids are taken regularly over a period of time, but that the risk of addiction is relatively low, although estimates do vary. Discontinuing chronic opioid therapy may be difficult, even in the absence of addiction. According to the World Health Organization, "The development of tolerance and physical dependence denote normal physiologic adaptations of the body to the presence of an opioid" [70]. Consequently, physical dependence alone is neither necessary nor sufficient to diagnose addiction [71,72].

Diversion: Drug diversion is defined as the intentional transfer of a controlled substance from authorized to unauthorized possession or channels of distribution [73-74]. The federal Controlled Substances Act (21 U.S.C. §§ 801 et seq.) establishes a closed system of distribution for drugs that are classified as controlled substances. Records must be kept from the time a drug is manufactured to the time it is dispensed. Health care professionals who are authorized to prescribe, dispense, and otherwise control access to such drugs are required to register with the DEA [25,75].

Pharmaceuticals that make their way outside this closed distribution system are said to have been "diverted" [75], and the individuals responsible for the diversion (including patients) are in violation of federal law.

Experience shows that the degree to which a prescribed medication is misused depends in large part on how easily it is redirected (diverted) from the legitimate distribution system [17,19,74].

Misuse: The term *misuse* (also called *nonmedical use*) encompasses all uses of a prescription medication other than those that are directed by a physician and used by a patient within the law and the requirements of good medical practice [28].

Opioid: An opioid is any compound that binds to an opioid receptor in the central nervous system (CNS) [4]. The class includes both naturally occurring and synthetic or semi-synthetic opioid drugs or medications, as well as endogenous opioid peptides [35].

Most physicians use the terms "opiate" and "opioid" interchangeably, but toxicologists (who perform and interpret drug tests) make a clear distinction between them. "Opioid" is the broader term because it includes the entire class of agents that act at opioid receptors in the CNS, whereas "opiates" refers to natural compounds derived from the opium plant but not semisynthetic opioid derivatives of opiates or completely synthetic agents. Thus, drug tests that are "positive for opiates" have detected one of these compounds or a metabolite of heroin, 6-monoacetyl morphine (MAM). Drug tests that are "negative for opiates" have found no detectable levels of opiates in the sample, even though other opioids that were not tested for—including the most common currently used and misused prescription opioids—may be present in the sample that was analyzed [53,59-260].

Pain: An unpleasant and potentially disabling sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.

Acute pain is the normal, predictable physiological response to a noxious chemical, thermal or mechanical stimulus and typically is associated with invasive procedures, trauma and disease. Acute pain generally is time-limited, lasting six weeks or less [4].

Chronic pain is a state in which pain persists beyond the usual course of an acute disease or healing of an injury (e.g., more than three months). It may or may not be associated with an acute or chronic pathologic process that causes continuous or intermittent pain over a period of months or years.

Chronic non-cancer related pain is chronic pain that is not associated with active cancer and does not occur at the end of life [4,76].

Opioid-induced hyperalgesia may develop as a result of long-term opioid use in the treatment of chronic pain. *Primary hyperalgesia* is pain sensitivity that occurs directly in the damaged tissues, while *secondary hyperalgesia* occurs in surrounding undamaged tissues. Human and animal studies have demonstrated that primary or secondary hyperalgesia can develop in response to both chronic and acute exposure to opioids. Hyperalgesia can be severe enough to warrant discontinuation of opioid treatment [77].

Prescription Drug Monitoring Program: Almost all states have enacted laws that establish prescription drug monitoring programs (PDMPs) to facilitate the collection, analysis, and reporting of information on the prescribing and dispensing of controlled substances. Most such programs employ electronic data transfer systems, under which prescription information is transmitted from the dispensing pharmacy to a state agency, which collates and analyzes the information [3,24].

After analyzing the efficacy of PDMPs, the GAO concluded that such programs have the potential to help law enforcement and regulatory agencies rapidly identify and investigate activities that may involve illegal prescribing, dispensing or consumption of controlled substances. Where real-time data are available, PDMPs also can help to prevent prescription drug misuse and diversion by allowing physicians to determine whether a patient is receiving prescriptions for controlled substances from other physicians, as well as whether the patient has filled or refilled an order for an opioid the physician has prescribed [24,78-79].

Tolerance: Tolerance is a state of physiologic adaptation in which exposure to a drug induces changes that result in diminution of one or more of the drug's effects over time. Tolerance is common in opioid treatment, has been demonstrated following a single dose of opioids, and is not the same as addiction [28].

Trial Period: A period of time during which the efficacy of an opioid for treatment of an individual's pain is tested to determine whether the treatment goals can be met in terms of reduction of pain and restoration of function. If the goals are not met, the opioid dose may be adjusted, a different opioid substituted, an adjunctive therapy added, or use of opioids discontinued and an alternative approach to pain management selected [36].

Universal Precautions: The concept of *universal precautions* is borrowed from an infectious disease model of the same name to underscore its comparability to practices in other areas of medicine. The concept recognizes that all patients have a level of risk that can only be estimated initially, with the estimate modified over time as more information is obtained. The 10 essential steps of universal precautions can be summarized as follows [38]:

1. Make a diagnosis with an appropriate differential.
2. Conduct a patient assessment, including risk for substance use disorders.
3. Discuss the proposed treatment plan with the patient and obtain informed consent.
4. Have a written treatment agreement that sets forth the expectations and obligations of both the patient and the rreating physician.
5. Initiate an appropriate trial of opioid therapy, with or without adjunctive medications.
6. Perform regular assessments of pain and function.
7. Reassess the patient's pain score and level of function.
8. Regularly evaluate the patient in terms of the "5 A's": Analgesia, Activity, Adverse effects, Aberrant behaviors, and Affect.
9. Periodically review the pain diagnosis and any comorbid conditions, including substance use disorders, and adjust the treatment regimen accordingly.
10. Keep careful and complete records of the initial evaluation and each follow-up visit.

By acknowledging the fact that there are no signs that invariably point to substance use disorder [41], the universal precautions encourage a consistent and respectful approach to the assessment and management of pain patients, thereby minimizing stigma, improving patient care, and reducing overall risk [38].

DRAFT Regulations for Pain Management

(NOTE: All of section 95 is new language and will be underlined)

18VAC85-20-95. Treatment of pain with controlled substances

A. Definitions. For purposes of this section, the following words and terms shall have the following meanings:

"Acute pain" shall mean pain that occurs within the normal course of a disease or condition or as the result of surgery for which controlled substances may be prescribed for no more than six months.

"Chronic pain" shall mean non-malignant pain that goes beyond the normal course of a disease or condition for which controlled substances may be prescribed for a period greater than six months.

"Controlled substance" shall mean drugs listed in The Drug Control Act of the Code of Virginia in Schedules II through IV.

"Prescription Monitoring Program" shall mean the electronic system within the Department of Health Professions that monitors the dispensing of certain controlled substances.

B. Treatment of acute pain

1. Evaluation of the patient.

Prior to initiating treatment with a controlled substance for a complaint of acute pain, the prescriber shall perform a history and physical examination appropriate to the complaint.

2. Medical records.

The medical record shall include a description of the pain, a presumptive diagnosis for the origin of the pain, an examination appropriate to the complaint, a treatment plan and the medication prescribed (including date, type, dosage and quantity prescribed).

C. Management of chronic pain

1. Evaluation of the patient

Prior to initiating management of chronic pain with a controlled substance, a medical history and physical examination shall be performed and documented in the medical record, including: a) the nature and intensity of the pain; b) current and past treatments for pain; c) underlying or coexisting diseases or conditions; d) the effect of the pain on physical and psychological and social function; e) psychiatric, addiction and substance abuse history of the patient and his family; f) and a urine drug screen. The medical record

also shall document the presence of one or more recognized medical indications for the use of a controlled substance.

3. Treatment plan.

The medical record shall include a treatment plan that states measures to be used to determine progress in treatment, including but not limited to pain relief and improved physical and psychosocial function. The treatment plan shall include further diagnostic evaluations and other treatment modalities or rehabilitation that may be necessary depending on the etiology of the pain and the extent to which the pain is associated with physical and psychosocial impairment. The prescriber shall record in the patient records the presence or absence of any indicators for medication misuse, abuse or diversion.

4. Informed consent and agreement for treatment.

The prescriber shall document in the medical record informed consent, to include risks, benefits and alternative approaches, prior to the initiation of opioids for chronic pain. There shall be a written treatment agreement in the medical record that addresses the parameters of treatment, including those behaviors which will result in a cessation of treatment or dismissal from care. The treatment agreement shall include, but not be limited to permission for the practitioner to: a) obtain urine/serum medication levels, when requested; b) query and receive reports from the Prescription Monitoring Program; and c) consult with other prescribers or dispensing pharmacists for the patient.

5. Periodic review.

The prescriber shall review the course of pain treatment and any new information about the etiology of the pain or the patient's state of health at least every six months. Continuation of treatment with controlled substances shall be supported by documentation of continued benefit from the prescribing. If the patient's progress is unsatisfactory, the prescriber shall assess the appropriateness of continued use of the current treatment plan and consider the use of other therapeutic modalities.

6. Consultation.

When necessary to achieve treatment goals, the prescriber shall refer the patient for additional evaluation and treatment.

7. Medical records.

The prescriber shall keep current, accurate and complete records in an accessible manner and readily available for review to include:

a. The medical history and physical examination;

b. Past medical history;

c. Records from prior treatment providers;

d. Diagnostic, therapeutic and laboratory results;

e. Evaluations and consultations;

f. Treatment goals;

g. Discussion of risks and benefits;

h. Informed consent and agreement for treatment;

i. Treatments;

j. Medications (including date, type, dosage and quantity prescribed). During the course of treatment, the physician shall adjust drug therapy to the individual medical needs of the patient and record the rationale for adjustments. Records shall document the medical necessity for any prescriptions in excess of recommended dosage in accordance with §§ 54.1-2971.01 and 54.1-3408.1 of the Code of Virginia;

k. Instructions and agreements; and

l. Periodic reviews.

REVISED: May 29, 2007

CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016

Recommendations and Reports / March 18, 2016 / 65(1);1–49

The following "Recommendations" are an excerpt of the full CDC Guideline which can be found at https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm
The full document includes the evidence reviewed, acknowledgements, and references.

Recommendations

The recommendations are grouped into three areas for consideration:

- Determining when to initiate or continue opioids for chronic pain.
- Opioid selection, dosage, duration, follow-up, and discontinuation.
- Assessing risk and addressing harms of opioid use.

There are 12 recommendations (Box 1). Each recommendation is followed by a rationale for the recommendation, with considerations for implementation noted. In accordance with the ACIP GRADE process, CDC based the recommendations on consideration of the clinical evidence, contextual evidence (including benefits and harms, values and preferences, resource allocation), and expert opinion. For each recommendation statement, CDC notes the recommendation category (A or B) and the type of the evidence (1, 2, 3, or 4) supporting the statement (Box 2). Expert opinion is reflected within each of the recommendation rationales. While there was not an attempt to reach consensus among experts, experts from the Core Expert Group and from the Opioid Guideline Workgroup ("experts") expressed overall, general support for all recommendations. Where differences in expert opinion emerged for detailed actions within the clinical recommendations or for implementation considerations, CDC notes the differences of opinion in the supporting rationale statements.

Category A recommendations indicate that most patients should receive the recommended course of action; category B recommendations indicate that different choices will be appropriate for different patients, requiring clinicians to help patients arrive at a decision consistent with patient values and preferences and specific clinical situations. Consistent with the ACIP (*47*) and GRADE process (*48*), category A recommendations were made, even with type 3 and 4 evidence, when there was broad

agreement that the advantages of a clinical action greatly outweighed the disadvantages based on a consideration of benefits and harms, values and preferences, and resource allocation. Category B recommendations were made when there was broad agreement that the advantages and disadvantages of a clinical action were more balanced, but advantages were significant enough to warrant a recommendation. All recommendations are category A recommendations, with the exception of recommendation 10, which is rated as category B. Recommendations were associated with a range of evidence types, from type 2 to type 4.

In summary, the categorization of recommendations was based on the following assessment:

- No evidence shows a long-term benefit of opioids in pain and function versus no opioids for chronic pain with outcomes examined at least 1 year later (with most placebo-controlled randomized trials ≤6 weeks in duration).
- Extensive evidence shows the possible harms of opioids (including opioid use disorder, overdose, and motor vehicle injury).
- Extensive evidence suggests some benefits of nonpharmacologic and nonopioid pharmacologic treatments compared with long-term opioid therapy, with less harm.

Determining When to Initiate or Continue Opioids for Chronic Pain

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate (recommendation category: A, evidence type: 3).

Patients with pain should receive treatment that provides the greatest benefits relative to risks. The contextual evidence review found that many nonpharmacologic therapies, including physical therapy, weight loss for knee osteoarthritis, psychological therapies such as CBT, and certain interventional procedures can ameliorate chronic pain. There is high-quality evidence that exercise therapy (a prominent modality in physical therapy) for hip (*100*) or knee (*99*) osteoarthritis reduces pain and improves function immediately after treatment and that the improvements are sustained for at least 2–6 months. Previous guidelines have strongly recommended aerobic, aquatic, and/or resistance exercises for patients with osteoarthritis of the knee or hip (*176*). Exercise therapy also can help reduce pain and improve function in low back pain and can improve global well-being and physical function in fibromyalgia (*98,101*). Multimodal therapies and multidisciplinary biopsychosocial

rehabilitation-combining approaches (e.g., psychological therapies with exercise) can reduce long-term pain and disability compared with usual care and compared with physical treatments (e.g., exercise) alone. Multimodal therapies are not always available or reimbursed by insurance and can be time-consuming and costly for patients. Interventional approaches such as arthrocentesis and intraarticular glucocorticoid injection for pain associated with rheumatoid arthritis (*117*) or osteoarthritis (*118*) and subacromial corticosteroid injection for rotator cuff disease (*119*) can provide short-term improvement in pain and function. Evidence is insufficient to determine the extent to which repeated glucocorticoid injection increases potential risks such as articular cartilage changes (in osteoarthritis) and sepsis (*118*). Serious adverse events are rare but have been reported with epidural injection (*120*).

Several nonopioid pharmacologic therapies (including acetaminophen, NSAIDs, and selected antidepressants and anticonvulsants) are effective for chronic pain. In particular, acetaminophen and NSAIDs can be useful for arthritis and low back pain. Selected anticonvulsants such as pregabalin and gabapentin can improve pain in diabetic neuropathy and post-herpetic neuralgia (contextual evidence review). Pregabalin, gabapentin, and carbamazepine are FDA-approved for treatment of certain neuropathic pain conditions, and pregabalin is FDA approved for fibromyalgia management. In patients with or without depression, tricyclic antidepressants and SNRIs provide effective analgesia for neuropathic pain conditions including diabetic neuropathy and post-herpetic neuralgia, often at lower dosages and with a shorter time to onset of effect than for treatment of depression (see contextual evidence review). Tricyclics and SNRIs can also relieve fibromyalgia symptoms. The SNRI duloxetine is FDA-approved for the treatment of diabetic neuropathy and fibromyalgia. Because patients with chronic pain often suffer from concurrent depression (*144*), and depression can exacerbate physical symptoms including pain (*177*), patients with co-occurring pain and depression are especially likely to benefit from antidepressant medication (see Recommendation 8). Nonopioid pharmacologic therapies are not generally associated with substance use disorder, and the numbers of fatal overdoses associated with nonopioid medications are a fraction of those associated with opioid medications (contextual evidence review). For example, acetaminophen, NSAIDs, and opioid pain medication were involved in 881, 228, and 16,651 pharmaceutical overdose deaths in the United States in 2010 (*178*). However, nonopioid pharmacologic therapies are associated with certain risks, particularly in older patients, pregnant patients, and patients with certain co-morbidities such as cardiovascular, renal, gastrointestinal, and liver disease (see contextual evidence review). For example, acetaminophen can be hepatotoxic at dosages of > 3-4 grams/day and at lower dosages in patients with chronic alcohol use or liver disease (*109*). NSAID use has been associated with gastritis, peptic ulcer disease, cardiovascular events (*111*,*112*), and

fluid retention, and most NSAIDs (choline magnesium trilisate and selective COX-2 inhibitors are exceptions) interfere with platelet aggregation (*179*). Clinicians should review FDA-approved labeling including boxed warnings before initiating treatment with any pharmacologic therapy.

Although opioids can reduce pain during short-term use, the clinical evidence review found insufficient evidence to determine whether pain relief is sustained and whether function or quality of life improves with long-term opioid therapy (KQ1). While benefits for pain relief, function, and quality of life with long-term opioid use for chronic pain are uncertain, risks associated with long-term opioid use are clearer and significant. Based on the clinical evidence review, long-term opioid use for chronic pain is associated with serious risks including increased risk for opioid use disorder, overdose, myocardial infarction, and motor vehicle injury (KQ2). At a population level, more than 165,000 persons in the United States have died from opioid pain-medication-related overdoses since 1999 (see Contextual Evidence Review).

Integrated pain management requires coordination of medical, psychological, and social aspects of health care and includes primary care, mental health care, and specialist services when needed (*180*). Nonpharmacologic physical and psychological treatments such as exercise and CBT are approaches that encourage active patient participation in the care plan, address the effects of pain in the patient's life, and can result in sustained improvements in pain and function without apparent risks. Despite this, these therapies are not always or fully covered by insurance, and access and cost can be barriers for patients. For many patients, aspects of these approaches can be used even when there is limited access to specialty care. For example, previous guidelines have strongly recommended aerobic, aquatic, and/or resistance exercises for patients with osteoarthritis of the knee or hip (*176*) and maintenance of activity for patients with low back pain (*110*). A randomized trial found no difference in reduced chronic low back pain intensity, frequency or disability between patients assigned to relatively low-cost group aerobics and individual physiotherapy or muscle reconditioning sessions (*181*). Low-cost options to integrate exercise include brisk walking in public spaces or use of public recreation facilities for group exercise. CBT addresses psychosocial contributors to pain and improves function (*97*). Primary care clinicians can integrate elements of a cognitive behavioral approach into their practice by encouraging patients to take an active role in the care plan, by supporting patients in engaging in beneficial but potentially anxiety-provoking activities, such as exercise (*179*), or by providing education in relaxation techniques and coping strategies. In many locations, there are free or low-cost patient support, self-help, and educational community-based programs that can provide stress reduction and other mental health benefits. Patients with more entrenched anxiety or fear related to pain, or other significant psychological distress, can be

referred for formal therapy with a mental health specialist (e.g., psychologist, psychiatrist, clinical social worker). Multimodal therapies should be considered for patients not responding to single-modality therapy, and combinations should be tailored depending on patient needs, cost, and convenience.

To guide patient-specific selection of therapy, clinicians should evaluate patients and establish or confirm the diagnosis. Detailed recommendations on diagnosis are provided in other guidelines (*110*,*179*), but evaluation should generally include a focused history, including history and characteristics of pain and potentially contributing factors (e.g., function, psychosocial stressors, sleep) and physical exam, with imaging or other diagnostic testing only if indicated (e.g., if severe or progressive neurologic deficits are present or if serious underlying conditions are suspected) (*110*,*179*). For complex pain syndromes, pain specialty consultation can be considered to assist with diagnosis as well as management. Diagnosis can help identify disease-specific interventions to reverse or ameliorate pain; for example, improving glucose control to prevent progression of diabetic neuropathy; immune-modulating agents for rheumatoid arthritis; physical or occupational therapy to address posture, muscle weakness, or repetitive occupational motions that contribute to musculoskeletal pain; or surgical intervention to relieve mechanical/compressive pain (*179*). The underlying mechanism for most pain syndromes can be categorized as neuropathic (e.g., diabetic neuropathy, postherpetic neuralgia, fibromyalgia), or nociceptive (e.g., osteoarthritis, muscular back pain). The diagnosis and pathophysiologic mechanism of pain have implications for symptomatic pain treatment with medication. For example, evidence is limited or insufficient for improved pain or function with long-term use of opioids for several chronic pain conditions for which opioids are commonly prescribed, such as low back pain (*182*), headache (*183*), and fibromyalgia (*184*). Although NSAIDs can be used for exacerbations of nociceptive pain, other medications (e.g., tricyclics, selected anticonvulsants, or transdermal lidocaine) generally are recommended for neuropathic pain. In addition, improvement of neuropathic pain can begin weeks or longer after symptomatic treatment is initiated (*179*). Medications should be used only after assessment and determination that expected benefits outweigh risks given patient-specific factors. For example, clinicians should consider falls risk when selecting and dosing potentially sedating medications such as tricyclics, anticonvulsants, or opioids, and should weigh risks and benefits of use, dose, and duration of NSAIDs when treating older adults as well as patients with hypertension, renal insufficiency, or heart failure, or those with risk for peptic ulcer disease or cardiovascular disease. Some guidelines recommend topical NSAIDs for localized osteoarthritis (e.g., knee osteoarthritis) over oral NSAIDs in patients aged ≥ 75 years to minimize systemic effects (*176*).

Experts agreed that opioids should not be considered first-line or routine therapy for chronic pain (i.e., pain continuing or expected to continue >3 months or past the time of normal tissue healing) outside of active cancer, palliative, and end-of-life care, given small to moderate short-term benefits, uncertain long-term benefits, and potential for serious harms; although evidence on long-term benefits of nonopioid therapies is also limited, these therapies are also associated with short-term benefits, and risks are much lower. This does not mean that patients should be required to sequentially "fail" nonpharmacologic and nonopioid pharmacologic therapy before proceeding to opioid therapy. Rather, expected benefits specific to the clinical context should be weighed against risks before initiating therapy. In some clinical contexts (e.g., headache or fibromyalgia), expected benefits of initiating opioids are unlikely to outweigh risks regardless of previous nonpharmacologic and nonopioid pharmacologic therapies used. In other situations (e.g., serious illness in a patient with poor prognosis for return to previous level of function, contraindications to other therapies, and clinician and patient agreement that the overriding goal is patient comfort), opioids might be appropriate regardless of previous therapies used. In addition, when opioid pain medication is used, it is more likely to be effective if integrated with nonpharmacologic therapy. Nonpharmacologic approaches such as exercise and CBT should be used to reduce pain and improve function in patients with chronic pain. Nonopioid pharmacologic therapy should be used when benefits outweigh risks and should be combined with nonpharmacologic therapy to reduce pain and improve function. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate, to provide greater benefits to patients in improving pain and function.

2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how opioid therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety (recommendation category: A, evidence type: 4).

The clinical evidence review found insufficient evidence to determine long-term benefits of opioid therapy for chronic pain and found an increased risk for serious harms related to long-term opioid therapy that appears to be dose-dependent. In addition, studies on currently available risk assessment instruments were sparse and showed inconsistent results (KQ4). The clinical evidence review for the current guideline considered studies with outcomes examined at ≥1 year that compared opioid use versus nonuse or placebo. Studies of opioid therapy for chronic pain that did not have a nonopioid control group have found that although many patients discontinue opioid

therapy for chronic noncancer pain due to adverse effects or insufficient pain relief, there is weak evidence that patients who are able to continue opioid therapy for at least 6 months can experience clinically significant pain relief and insufficient evidence that function or quality of life improves (*185*). These findings suggest that it is very difficult for clinicians to predict whether benefits of opioids for chronic pain will outweigh risks of ongoing treatment for individual patients. Opioid therapy should not be initiated without consideration of an "exit strategy" to be used if the therapy is unsuccessful.

Experts agreed that before opioid therapy is initiated for chronic pain outside of active cancer, palliative, and end-of-life care, clinicians should determine how effectiveness will be evaluated and should establish treatment goals with patients. Because the line between acute pain and initial chronic pain is not always clear, it might be difficult for clinicians to determine when they are initiating opioids for chronic pain rather than treating acute pain. Pain lasting longer than 3 months or past the time of normal tissue healing (which could be substantially shorter than 3 months, depending on the condition) is generally no longer considered acute. However, establishing treatment goals with a patient who has already received opioid therapy for 3 months would defer this discussion well past the point of initiation of opioid therapy for chronic pain. Clinicians often write prescriptions for long-term use in 30-day increments, and opioid prescriptions written for ≥30 days are likely to represent initiation or continuation of long-term opioid therapy. Before writing an opioid prescription for ≥30 days, clinicians should establish treatment goals with patients. Clinicians seeing new patients already receiving opioids should establish treatment goals for continued opioid therapy. Although the clinical evidence review did not find studies evaluating the effectiveness of written agreements or treatment plans (KQ4), clinicians and patients who set a plan in advance will clarify expectations regarding how opioids will be prescribed and monitored, as well as situations in which opioids will be discontinued or doses tapered (e.g., if treatment goals are not met, opioids are no longer needed, or adverse events put the patient at risk) to improve patient safety.

Experts thought that goals should include improvement in both pain relief and function (and therefore in quality of life). However, there are some clinical circumstances under which reductions in pain without improvement in physical function might be a more realistic goal (e.g., diseases typically associated with progressive functional impairment or catastrophic injuries such as spinal cord trauma). Experts noted that function can include emotional and social as well as physical dimensions. In addition, experts emphasized that mood has important interactions with pain and function. Experts agreed that clinicians may use validated instruments such as the three-item "Pain average, interference with Enjoyment of life, and interference with General activity" (PEG) Assessment Scale (*186*) to track patient outcomes. Clinically meaningful improvement has been

defined as a 30% improvement in scores for both pain and function (*187*). Monitoring progress toward patient-centered functional goals (e.g., walking the dog or walking around the block, returning to part-time work, attending family sports or recreational activities) can also contribute to the assessment of functional improvement. Clinicians should use these goals in assessing benefits of opioid therapy for individual patients and in weighing benefits against risks of continued opioid therapy (see Recommendation 7, including recommended intervals for follow-up). Because depression, anxiety, and other psychological co-morbidities often coexist with and can interfere with resolution of pain, clinicians should use validated instruments to assess for these conditions (see Recommendation 8) and ensure that treatment for these conditions is optimized. If patients receiving opioid therapy for chronic pain do not experience meaningful improvements in both pain and function compared with prior to initiation of opioid therapy, clinicians should consider working with patients to taper and discontinue opioids (see Recommendation 7) and should use nonpharmacologic and nonopioid pharmacologic approaches to pain management (see Recommendation 1).

3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy (recommendation category: A, evidence type: 3).

The clinical evidence review did not find studies evaluating effectiveness of patient education or opioid treatment plans as risk-mitigation strategies (KQ4). However, the contextual evidence review found that many patients lack information about opioids and identified concerns that some clinicians miss opportunities to effectively communicate about safety. Given the substantial evidence gaps on opioids, uncertain benefits of long-term use, and potential for serious harms, patient education and discussion before starting opioid therapy are critical so that patient preferences and values can be understood and used to inform clinical decisions. Experts agreed that essential elements to communicate to patients before starting and periodically during opioid therapy include realistic expected benefits, common and serious harms, and expectations for clinician and patient responsibilities to mitigate risks of opioid therapy.

Clinicians should involve patients in decisions about whether to start or continue opioid therapy. Given potentially serious risks of long-term opioid therapy, clinicians should ensure that patients are aware of potential benefits of, harms of, and alternatives to opioids before starting or continuing opioid therapy. Clinicians are encouraged to have open and honest discussions with patients to inform mutual decisions about whether to start or continue opioid therapy. Important considerations include the following:

- Be explicit and realistic about expected benefits of opioids, explaining that while opioids can reduce pain during short-term use, there is no good evidence that opioids improve pain or function with long-term use, and that complete relief of pain is unlikely (clinical evidence review, KQ1).
- Emphasize improvement in function as a primary goal and that function can improve even when pain is still present.
- Advise patients about serious adverse effects of opioids, including potentially fatal respiratory depression and development of a potentially serious lifelong opioid use disorder that can cause distress and inability to fulfill major role obligations.
- Advise patients about common effects of opioids, such as constipation, dry mouth, nausea, vomiting, drowsiness, confusion, tolerance, physical dependence, and withdrawal symptoms when stopping opioids. To prevent constipation associated with opioid use, advise patients to increase hydration and fiber intake and to maintain or increase physical activity. Stool softeners or laxatives might be needed.
- Discuss effects that opioids might have on ability to safely operate a vehicle, particularly when opioids are initiated, when dosages are increased, or when other central nervous system depressants, such as benzodiazepines or alcohol, are used concurrently.
- Discuss increased risks for opioid use disorder, respiratory depression, and death at higher dosages, along with the importance of taking only the amount of opioids prescribed, i.e., not taking more opioids or taking them more often.
- Review increased risks for respiratory depression when opioids are taken with benzodiazepines, other sedatives, alcohol, illicit drugs such as heroin, or other opioids.
- Discuss risks to household members and other individuals if opioids are intentionally or unintentionally shared with others for whom they are not prescribed, including the possibility that others might experience overdose at the same or at lower dosage than prescribed for the patient, and that young children are susceptible to unintentional ingestion. Discuss storage of opioids in a secure, preferably locked location and options for safe disposal of unused opioids (*188*).
- Discuss the importance of periodic reassessment to ensure that opioids are helping to meet patient goals and to allow opportunities for opioid discontinuation and consideration of additional nonpharmacologic or nonopioid pharmacologic treatment options if opioids are not effective or are harmful.
- Discuss planned use of precautions to reduce risks, including use of prescription drug monitoring program information (see Recommendation 9) and urine drug testing (see Recommendation 10). Consider including discussion of naloxone use for overdose reversal (see Recommendation 8).

- Consider whether cognitive limitations might interfere with management of opioid therapy (for older adults in particular) and, if so, determine whether a caregiver can responsibly co-manage medication therapy. Discuss the importance of reassessing safer medication use with both the patient and caregiver.

Given the possibility that benefits of opioid therapy might diminish or that risks might become more prominent over time, it is important that clinicians review expected benefits and risks of continued opioid therapy with patients periodically, at least every 3 months (see Recommendation 7).

Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids (recommendation category: A, evidence type: 4).

ER/LA opioids include methadone, transdermal fentanyl, and extended-release versions of opioids such as oxycodone, oxymorphone, hydrocodone, and morphine. The clinical evidence review found a fair-quality study showing a higher risk for overdose among patients initiating treatment with ER/LA opioids than among those initiating treatment with immediate-release opioids (*77*). The clinical evidence review did not find evidence that continuous, time-scheduled use of ER/LA opioids is more effective or safer than intermittent use of immediate-release opioids or that time-scheduled use of ER/LA opioids reduces risks for opioid misuse or addiction (KQ3).

In 2014, the FDA modified the labeling for ER/LA opioid pain medications, noting serious risks and recommending that ER/LA opioids be reserved for "management of pain severe enough to require daily, around-the-clock, long-term opioid treatment" when "alternative treatment options (e.g., nonopioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain" and not used as "as needed" pain relievers (*121*). FDA has also noted that some ER/LA opioids are only appropriate for opioid-tolerant patients, defined as patients who have received certain dosages of opioids (e.g., 60 mg daily of oral morphine, 30 mg daily of oral oxycodone, or equianalgesic dosages of other opioids) for at least 1 week (*189*). Time-scheduled opioid use can be associated with greater total average daily opioid dosage compared with intermittent, as-needed opioid use (contextual evidence review). In addition, experts indicated that there was not enough evidence to determine the safety of using immediate-release opioids for breakthrough pain when ER/LA opioids are used for chronic pain outside of active cancer pain, palliative care, or end-of-life care, and that this practice might be associated with dose escalation.

Abuse-deterrent technologies have been employed to prevent manipulation intended to defeat extended-release properties of ER/LA opioids and to prevent opioid use by unintended routes of administration, such as injection of oral opioids. As indicated in FDA guidance for industry on evaluation and labeling of abuse-deterrent opioids (*190*), although abuse-deterrent technologies are expected to make manipulation of opioids more difficult or less rewarding, they do not prevent opioid abuse through oral intake, the most common route of opioid abuse, and can still be abused by nonoral routes. The "abuse-deterrent" label does not indicate that there is no risk for abuse. No studies were found in the clinical evidence review assessing the effectiveness of abuse-deterrent technologies as a risk mitigation strategy for deterring or preventing abuse. In addition, abuse-deterrent technologies do not prevent unintentional overdose through oral intake. Experts agreed that recommendations could not be offered at this time related to use of abuse-deterrent formulations.

In comparing different ER/LA formulations, the clinical evidence review found inconsistent results for overdose risk with methadone versus other ER/LA opioids used for chronic pain (KQ3). The contextual evidence review found that methadone has been associated with disproportionate numbers of overdose deaths relative to the frequency with which it is prescribed for chronic pain. In addition, methadone is associated with cardiac arrhythmias along with QT prolongation on the electrocardiogram, and it has complicated pharmacokinetics and pharmacodynamics, including a long and variable half-life and peak respiratory depressant effect occurring later and lasting longer than peak analgesic effect. Experts noted that the pharmacodynamics of methadone are subject to more inter-individual variability than other opioids. In regard to other ER/LA opioid formulations, experts noted that the absorption and pharmacodynamics of transdermal fentanyl are complex, with gradually increasing serum concentration during the first part of the 72-hour dosing interval, as well as variable absorption based on factors such as external heat. In addition, the dosing of transdermal fentanyl in mcg/hour, which is not typical for a drug used by outpatients, can be confusing. Experts thought that these complexities might increase the risk for fatal overdose when methadone or transdermal fentanyl is prescribed to a patient who has not used it previously or by clinicians who are not familiar with its effects.

Experts agreed that for patients not already receiving opioids, clinicians should not initiate opioid treatment with ER/LA opioids and should not prescribe ER/LA opioids for intermittent use. ER/LA opioids should be reserved for severe, continuous pain and should be considered only for patients who have received immediate-release opioids daily for at least 1 week. When changing to an ER/LA opioid for a patient previously receiving a different immediate-release opioid, clinicians should

consult product labeling and reduce total daily dosage to account for incomplete opioid cross-tolerance. Clinicians should use additional caution with ER/LA opioids and consider a longer dosing interval when prescribing to patients with renal or hepatic dysfunction because decreased clearance of drugs among these patients can lead to accumulation of drugs to toxic levels and persistence in the body for longer durations. Although there might be situations in which clinicians need to prescribe immediate-release and ER/LA opioids together (e.g., transitioning patients from ER/LA opioids to immediate-release opioids by temporarily using lower dosages of both), in general, avoiding the use of immediate-release opioids in combination with ER/LA opioids is preferable, given potentially increased risk and diminishing returns of such an approach for chronic pain.

When an ER/LA opioid is prescribed, using one with predictable pharmacokinetics and pharmacodynamics is preferred to minimize unintentional overdose risk. In particular, unusual characteristics of methadone and of transdermal fentanyl make safe prescribing of these medications for pain especially challenging.

- Methadone should not be the first choice for an ER/LA opioid. Only clinicians who are familiar with methadone's unique risk profile and who are prepared to educate and closely monitor their patients, including risk assessment for QT prolongation and consideration of electrocardiographic monitoring, should consider prescribing methadone for pain. A clinical practice guideline that contains further guidance regarding methadone prescribing for pain has been published previously (*191*).
- Because dosing effects of transdermal fentanyl are often misunderstood by both clinicians and patients, only clinicians who are familiar with the dosing and absorption properties of transdermal fentanyl and are prepared to educate their patients about its use should consider prescribing it.

5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when considering increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day (recommendation category: A, evidence type: 3).

Benefits of high-dose opioids for chronic pain are not established. The clinical evidence review found only one study (*84*) addressing effectiveness of dose titration for outcomes related to pain control, function, and quality of life (KQ3). This randomized trial found no difference in pain or function between a more liberal opioid dose escalation strategy and maintenance of current dosage. (These groups were prescribed average dosages of 52 and 40 MME/day, respectively, at the end of the

trial.) At the same time, risks for serious harms related to opioid therapy increase at higher opioid dosage. The clinical evidence review found that higher opioid dosages are associated with increased risks for motor vehicle injury, opioid use disorder, and overdose (KQ2). The clinical and contextual evidence reviews found that opioid overdose risk increases in a dose-response manner, that dosages of 50–<100 MME/day have been found to increase risks for opioid overdose by factors of 1.9 to 4.6 compared with dosages of 1–<20 MME/day, and that dosages ≥100 MME/day are associated with increased risks of overdose 2.0–8.9 times the risk at 1–<20 MME/day. In a national sample of Veterans Health Administration patients with chronic pain who were prescribed opioids, mean prescribed opioid dosage among patients who died from opioid overdose was 98 MME (median 60 MME) compared with mean prescribed opioid dosage of 48 MME (median 25 MME) among patients not experiencing fatal overdose (*127*).

The contextual evidence review found that although there is not a single dosage threshold below which overdose risk is eliminated, holding dosages <50 MME/day would likely reduce risk among a large proportion of patients who would experience fatal overdose at higher prescribed dosages. Experts agreed that lower dosages of opioids reduce the risk for overdose, but that a single dosage threshold for safe opioid use could not be identified. Experts noted that daily opioid dosages close to or greater than 100 MME/day are associated with significant risks, that dosages <50 MME/day are safer than dosages of 50–100 MME/day, and that dosages <20 MME/day are safer than dosages of 20–50 MME/day. One expert thought that a specific dosage at which the benefit/risk ratio of opioid therapy decreases could not be identified. Most experts agreed that, in general, increasing dosages to 50 or more MME/day increases overdose risk without necessarily adding benefits for pain control or function and that clinicians should carefully reassess evidence of individual benefits and risks when considering increasing opioid dosages to ≥50 MME/day. Most experts also agreed that opioid dosages should not be increased to ≥90 MME/day without careful justification based on diagnosis and on individualized assessment of benefits and risks.

When opioids are used for chronic pain outside of active cancer, palliative, and end-of-life care, clinicians should start opioids at the lowest possible effective dosage (the lowest starting dosage on product labeling for patients not already taking opioids and according to product labeling guidance regarding tolerance for patients already taking opioids). Clinicians should use additional caution when initiating opioids for patients aged ≥65 years and for patients with renal or hepatic insufficiency because decreased clearance of drugs in these patients can result in accumulation of drugs to toxic levels. Clinicians should use caution when increasing opioid dosages and increase dosage by the smallest practical amount because overdose risk increases with increases in opioid dosage.

Although there is limited evidence to recommend specific intervals for dosage titration, a previous guideline recommended waiting at least five half-lives before increasing dosage and waiting at least a week before increasing dosage of methadone to make sure that full effects of the previous dosage are evident (*31*). Clinicians should re-evaluate patients after increasing dosage for changes in pain, function, and risk for harm (see Recommendation 7). Before increasing total opioid dosage to ≥50 MME/day, clinicians should reassess whether opioid treatment is meeting the patient's treatment goals (see Recommendation 2). If a patient's opioid dosage for all sources of opioids combined reaches or exceeds 50 MME/day, clinicians should implement additional precautions, including increased frequency of follow-up (see Recommendation 7) and considering offering naloxone and overdose prevention education to both patients and the patients' household members (see Recommendation 8). Clinicians should avoid increasing opioid dosages to ≥90 MME/day or should carefully justify a decision to increase dosage to ≥90 MME/day based on individualized assessment of benefits and risks and weighing factors such as diagnosis, incremental benefits for pain and function relative to harms as dosages approach 90 MME/day, other treatments and effectiveness, and recommendations based on consultation with pain specialists. If patients do not experience improvement in pain and function at ≥90 MME/day, or if there are escalating dosage requirements, clinicians should discuss other approaches to pain management with the patient, consider working with patients to taper opioids to a lower dosage or to taper and discontinue opioids (see Recommendation 7), and consider consulting a pain specialist. Some states require clinicians to implement clinical protocols at specific dosage levels. For example, before increasing long-term opioid therapy dosage to >120 MME/day, clinicians in Washington state must obtain consultation from a pain specialist who agrees that this is indicated and appropriate (*30*). Clinicians should be aware of rules related to MME thresholds and associated clinical protocols established by their states.

Established patients already taking high dosages of opioids, as well as patients transferring from other clinicians, might consider the possibility of opioid dosage reduction to be anxiety-provoking, and tapering opioids can be especially challenging after years on high dosages because of physical and psychological dependence. However, these patients should be offered the opportunity to re-evaluate their continued use of opioids at high dosages in light of recent evidence regarding the association of opioid dosage and overdose risk. Clinicians should explain in a nonjudgmental manner to patients already taking high opioid dosages (≥90 MME/day) that there is now an established body of scientific evidence showing that overdose risk is increased at higher opioid dosages. Clinicians should empathically review benefits and risks of continued high-dosage opioid therapy and should offer to work with the patient to taper opioids to safer dosages. For patients who

agree to taper opioids to lower dosages, clinicians should collaborate with the patient on a tapering plan (see Recommendation 7). Experts noted that patients tapering opioids after taking them for years might require very slow opioid tapers as well as pauses in the taper to allow gradual accommodation to lower opioid dosages. Clinicians should remain alert to signs of anxiety, depression, and opioid use disorder (see Recommendations 8 and 12) that might be unmasked by an opioid taper and arrange for management of these co-morbidities. For patients agreeing to taper to lower opioid dosages as well as for those remaining on high opioid dosages, clinicians should establish goals with the patient for continued opioid therapy (see Recommendation 2), maximize pain treatment with nonpharmacologic and nonopioid pharmacologic treatments as appropriate (see Recommendation 1), and consider consulting a pain specialist as needed to assist with pain management.

6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed (recommendation category: A, evidence type: 4).

The clinical evidence review found that opioid use for acute pain (i.e., pain with abrupt onset and caused by an injury or other process that is not ongoing) is associated with long-term opioid use, and that a greater amount of early opioid exposure is associated with greater risk for long-term use (KQ5). Several guidelines on opioid prescribing for acute pain from emergency departments (*192–194*) and other settings (*195*,*196*) have recommended prescribing ≤3 days of opioids in most cases, whereas others have recommended ≤7 days (*197*) or <14 days (*30*). Because physical dependence on opioids is an expected physiologic response in patients exposed to opioids for more than a few days (contextual evidence review), limiting days of opioids prescribed also should minimize the need to taper opioids to prevent distressing or unpleasant withdrawal symptoms. Experts noted that more than a few days of exposure to opioids significantly increases hazards, that each day of unnecessary opioid use increases likelihood of physical dependence without adding benefit, and that prescriptions with fewer days' supply will minimize the number of pills available for unintentional or intentional diversion.

Experts agreed that when opioids are needed for acute pain, clinicians should prescribe opioids at the lowest effective dose and for no longer than the expected duration of pain severe enough to require opioids to minimize unintentional initiation of long-term opioid use. The lowest effective dose can be determined using product labeling as a starting point with calibration as needed based on the

severity of pain and on other clinical factors such as renal or hepatic insufficiency (see Recommendation 8). Experts thought, based on clinical experience regarding anticipated duration of pain severe enough to require an opioid, that in most cases of acute pain not related to surgery or trauma, a ≤3 days' supply of opioids will be sufficient. For example, in one study of the course of acute low back pain (not associated with malignancies, infections, spondylarthropathies, fractures, or neurological signs) in a primary care setting, there was a large decrease in pain until the fourth day after treatment with paracetamol, with smaller decreases thereafter (*198*). Some experts thought that because some types of acute pain might require more than 3 days of opioid treatment, it would be appropriate to recommend a range of ≤3–5 days or ≤3–7 days when opioids are needed. Some experts thought that a range including 7 days was too long given the expected course of severe acute pain for most acute pain syndromes seen in primary care.

Acute pain can often be managed without opioids. It is important to evaluate the patient for reversible causes of pain, for underlying etiologies with potentially serious sequelae, and to determine appropriate treatment. When the diagnosis and severity of nontraumatic, nonsurgical acute pain are reasonably assumed to warrant the use of opioids, clinicians should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids, often 3 days or less, unless circumstances clearly warrant additional opioid therapy. More than 7 days will rarely be needed. Opioid treatment for post-surgical pain is outside the scope of this guideline but has been addressed elsewhere (*30*). Clinicians should not prescribe additional opioids to patients "just in case" pain continues longer than expected. Clinicians should re-evaluate the subset of patients who experience severe acute pain that continues longer than the expected duration to confirm or revise the initial diagnosis and to adjust management accordingly. Given longer half-lives and longer duration of effects (e.g., respiratory depression) with ER/LA opioids such as methadone, fentanyl patches, or extended release versions of opioids such as oxycodone, oxymorphone, or morphine, clinicians should not prescribe ER/LA opioids for the treatment of acute pain.

7. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids (recommendation category: A, evidence type: 4).

Although the clinical evidence review did not find studies evaluating the effectiveness of more frequent monitoring intervals (KQ4), it did find that continuing opioid therapy for 3 months substantially increases risk for opioid use disorder (KQ2); therefore, follow-up earlier than 3 months might be necessary to provide the greatest opportunity to prevent the development of opioid use disorder. In addition, risk for overdose associated with ER/LA opioids might be particularly high during the first 2 weeks of treatment (KQ3). The contextual evidence review found that patients who do not have pain relief with opioids at 1 month are unlikely to experience pain relief with opioids at 6 months. Although evidence is insufficient to determine at what point within the first 3 months of opioid therapy the risks for opioid use disorder increase, reassessment of pain and function within 1 month of initiating opioids provides an opportunity to minimize risks of long-term opioid use by discontinuing opioids among patients not receiving a clear benefit from these medications. Experts noted that risks for opioid overdose are greatest during the first 3–7 days after opioid initiation or increase in dosage, particularly when methadone or transdermal fentanyl are prescribed; that follow-up within 3 days is appropriate when initiating or increasing the dosage of methadone; and that follow-up within 1 week might be appropriate when initiating or increasing the dosage of other ER/LA opioids.

Clinicians should evaluate patients to assess benefits and harms of opioids within 1 to 4 weeks of starting long-term opioid therapy or of dose escalation. Clinicians should consider follow-up intervals within the lower end of this range when ER/LA opioids are started or increased or when total daily opioid dosage is ≥50 MME/day. Shorter follow-up intervals (within 3 days) should be strongly considered when starting or increasing the dosage of methadone. At follow up, clinicians should assess benefits in function, pain control, and quality of life using tools such as the three-item "Pain average, interference with Enjoyment of life, and interference with General activity" (PEG) Assessment Scale (*186*) and/or asking patients about progress toward functional goals that have meaning for them (see Recommendation 2). Clinicians should also ask patients about common adverse effects such as constipation and drowsiness (see Recommendation 3), as well as asking about and assessing for effects that might be early warning signs for more serious problems such as overdose (e.g., sedation or slurred speech) or opioid use disorder (e.g., craving, wanting to take opioids in greater quantities or more frequently than prescribed, or difficulty controlling use). Clinicians should ask patients about their preferences for continuing opioids, given their effects on pain and function relative to any adverse effects experienced.

Because of potential changes in the balance of benefits and risks of opioid therapy over time, clinicians should regularly reassess all patients receiving long-term opioid therapy, including patients

who are new to the clinician but on long-term opioid therapy, at least every 3 months. At reassessment, clinicians should determine whether opioids continue to meet treatment goals, including sustained improvement in pain and function, whether the patient has experienced common or serious adverse events or early warning signs of serious adverse events, signs of opioid use disorder (e.g., difficulty controlling use, work or family problems related to opioid use), whether benefits of opioids continue to outweigh risks, and whether opioid dosage can be reduced or opioids can be discontinued. Ideally, these reassessments would take place in person and be conducted by the prescribing clinician. In practice contexts where virtual visits are part of standard care (e.g., in remote areas where distance or other issues make follow-up visits challenging), follow-up assessments that allow the clinician to communicate with and observe the patient through video and audio could be conducted, with in-person visits occurring at least once per year. Clinicians should re-evaluate patients who are exposed to greater risk of opioid use disorder or overdose (e.g., patients with depression or other mental health conditions, a history of substance use disorder, a history of overdose, taking ≥50 MME/day, or taking other central nervous system depressants with opioids) more frequently than every 3 months. If clinically meaningful improvements in pain and function are not sustained, if patients are taking high-risk regimens (e.g., dosages ≥50 MME/day or opioids combined with benzodiazepines) without evidence of benefit, if patients believe benefits no longer outweigh risks or if they request dosage reduction or discontinuation, or if patients experience overdose or other serious adverse events (e.g., an event leading to hospitalization or disability) or warning signs of serious adverse events, clinicians should work with patients to reduce opioid dosage or to discontinue opioids when possible. Clinicians should maximize pain treatment with nonpharmacologic and nonopioid pharmacologic treatments as appropriate (see Recommendation 1) and consider consulting a pain specialist as needed to assist with pain management.

Considerations for Tapering Opioids

Although the clinical evidence review did not find high-quality studies comparing the effectiveness of different tapering protocols for use when opioid dosage is reduced or opioids are discontinued (KQ3), tapers reducing weekly dosage by 10%–50% of the original dosage have been recommended by other clinical guidelines (*199*), and a rapid taper over 2–3 weeks has been recommended in the case of a severe adverse event such as overdose (*30*). Experts noted that tapers slower than 10% per week (e.g., 10% per month) also might be appropriate and better tolerated than more rapid tapers, particularly when patients have been taking opioids for longer durations (e.g., for years). Opioid withdrawal during pregnancy has been associated with spontaneous abortion and premature labor.

When opioids are reduced or discontinued, a taper slow enough to minimize symptoms and signs of opioid withdrawal (e.g., drug craving, anxiety, insomnia, abdominal pain, vomiting, diarrhea, diaphoresis, mydriasis, tremor, tachycardia, or piloerection) should be used. A decrease of 10% of the original dose per week is a reasonable starting point; experts agreed that tapering plans may be individualized based on patient goals and concerns. Experts noted that at times, tapers might have to be paused and restarted again when the patient is ready and might have to be slowed once patients reach low dosages. Tapers may be considered successful as long as the patient is making progress. Once the smallest available dose is reached, the interval between doses can be extended. Opioids may be stopped when taken less frequently than once a day. More rapid tapers might be needed for patient safety under certain circumstances (e.g., for patients who have experienced overdose on their current dosage). Ultrarapid detoxification under anesthesia is associated with substantial risks, including death, and should not be used (*200*). Clinicians should access appropriate expertise if considering tapering opioids during pregnancy because of possible risk to the pregnant patient and to the fetus if the patient goes into withdrawal. Patients who are not taking opioids (including patients who are diverting all opioids they obtain) do not require tapers. Clinicians should discuss with patients undergoing tapering the increased risk for overdose on abrupt return to a previously prescribed higher dose. Primary care clinicians should collaborate with mental health providers and with other specialists as needed to optimize nonopioid pain management (see Recommendation 1), as well as psychosocial support for anxiety related to the taper. More detailed guidance on tapering, including management of withdrawal symptoms has been published previously (*30,201*). If a patient exhibits signs of opioid use disorder, clinicians should offer or arrange for treatment of opioid use disorder (see Recommendation 12) and consider offering naloxone for overdose prevention (see Recommendation 8).

Assessing Risk and Addressing Harms of Opioid Use

8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present (recommendation category: A, evidence type: 4).

The clinical evidence review found insufficient evidence to determine how harms of opioids differ depending on patient demographics or patient comorbidities (KQ2). However, based on the contextual evidence review and expert opinion, certain risk factors are likely to increase susceptibility

to opioid-associated harms and warrant incorporation of additional strategies into the management plan to mitigate risk. Clinicians should assess these risk factors periodically, with frequency varying by risk factor and patient characteristics. For example, factors that vary more frequently over time, such as alcohol use, require more frequent follow up. In addition, clinicians should consider offering naloxone, re-evaluating patients more frequently (see Recommendation 7), and referring to pain and/or behavioral health specialists when factors that increase risk for harm, such as history of overdose, history of substance use disorder, higher dosages of opioids (≥50 MME/day), and concurrent use of benzodiazepines with opioids, are present.

Patients with Sleep-Disordered Breathing, Including Sleep Apnea

Risk factors for sleep-disordered breathing include congestive heart failure, and obesity. Experts noted that careful monitoring and cautious dose titration should be used if opioids are prescribed for patients with mild sleep-disordered breathing. Clinicians should avoid prescribing opioids to patients with moderate or severe sleep-disordered breathing whenever possible to minimize risks for opioid overdose (contextual evidence review).

Pregnant Women

Opioids used in pregnancy might be associated with additional risks to both mother and fetus. Some studies have shown an association of opioid use in pregnancy with stillbirth, poor fetal growth, pre-term delivery, and birth defects (contextual evidence review). Importantly, in some cases, opioid use during pregnancy leads to neonatal opioid withdrawal syndrome. Clinicians and patients together should carefully weigh risks and benefits when making decisions about whether to initiate opioid therapy for chronic pain during pregnancy. In addition, before initiating opioid therapy for chronic pain for reproductive-age women, clinicians should discuss family planning and how long-term opioid use might affect any future pregnancy. For pregnant women already receiving opioids, clinicians should access appropriate expertise if considering tapering opioids because of possible risk to the pregnant patient and to the fetus if the patient goes into withdrawal (see Recommendation 7). For pregnant women with opioid use disorder, medication-assisted therapy with buprenorphine or methadone has been associated with improved maternal outcomes and should be offered (*202*) (see Recommendation 12). Clinicians caring for pregnant women receiving opioids for pain or receiving buprenorphine or methadone for opioid use disorder should arrange for delivery at a facility prepared to monitor, evaluate for, and treat neonatal opioid withdrawal syndrome. In instances when travel to such a facility would present an undue burden on the pregnant woman, it is appropriate to deliver locally, monitor and evaluate the newborn for neonatal opioid withdrawal syndrome, and transfer the

newborn for additional treatment if needed. Neonatal toxicity and death have been reported in breast-feeding infants whose mothers are taking codeine (contextual evidence review); previous guidelines have recommended that codeine be avoided whenever possible among mothers who are breast feeding and, if used, should be limited to the lowest possible dose and to a 4-day supply (*203*).

Patients with Renal or Hepatic Insufficiency

Clinicians should use additional caution and increased monitoring (see Recommendation 7) to minimize risks of opioids prescribed for patients with renal or hepatic insufficiency, given their decreased ability to process and excrete drugs, susceptibility to accumulation of opioids, and reduced therapeutic window between safe dosages and dosages associated with respiratory depression and overdose (contextual evidence review; see Recommendations 4, 5, and 7).

Patients Aged ≥65 Years

Inadequate pain treatment among persons aged ≥65 years has been documented (*204*). Pain management for older patients can be challenging given increased risks of both nonopioid pharmacologic therapies (see Recommendation 1) and opioid therapy in this population. Given reduced renal function and medication clearance even in the absence of renal disease, patients aged ≥65 years might have increased susceptibility to accumulation of opioids and a smaller therapeutic window between safe dosages and dosages associated with respiratory depression and overdose (contextual evidence review). Some older adults suffer from cognitive impairment, which can increase risk for medication errors and make opioid-related confusion more dangerous. In addition, older adults are more likely than younger adults to experience co-morbid medical conditions and more likely to receive multiple medications, some of which might interact with opioids (such as benzodiazepines). Clinicians should use additional caution and increased monitoring (see Recommendations 4, 5, and 7) to minimize risks of opioids prescribed for patients aged ≥65 years. Experts suggested that clinicians educate older adults receiving opioids to avoid risky medication-related behaviors such as obtaining controlled medications from multiple prescribers and saving unused medications. Clinicians should also implement interventions to mitigate common risks of opioid therapy among older adults, such as exercise or bowel regimens to prevent constipation, risk assessment for falls, and patient monitoring for cognitive impairment.

Patients with Mental Health Conditions

Because psychological distress frequently interferes with improvement of pain and function in patients with chronic pain, using validated instruments such as the Generalized Anxiety Disorder

(GAD)-7 and the Patient Health Questionnaire (PHQ)-9 or the PHQ-4 to assess for anxiety, post-traumatic stress disorder, and/or depression (*205*), might help clinicians improve overall pain treatment outcomes. Experts noted that clinicians should use additional caution and increased monitoring (see Recommendation 7) to lessen the increased risk for opioid use disorder among patients with mental health conditions (including depression, anxiety disorders, and PTSD), as well as increased risk for drug overdose among patients with depression. Previous guidelines have noted that opioid therapy should not be initiated during acute psychiatric instability or uncontrolled suicide risk, and that clinicians should consider behavioral health specialist consultation for any patient with a history of suicide attempt or psychiatric disorder (*31*). In addition, patients with anxiety disorders and other mental health conditions are more likely to receive benzodiazepines, which can exacerbate opioid-induced respiratory depression and increase risk for overdose (see Recommendation 11). Clinicians should ensure that treatment for depression and other mental health conditions is optimized, consulting with behavioral health specialists when needed. Treatment for depression can improve pain symptoms as well as depression and might decrease overdose risk (contextual evidence review). For treatment of chronic pain in patients with depression, clinicians should strongly consider using tricyclic or SNRI antidepressants for analgesic as well as antidepressant effects if these medications are not otherwise contraindicated (see Recommendation 1).

Patients with Substance Use Disorder

Illicit drugs and alcohol are listed as contributory factors on a substantial proportion of death certificates for opioid-related overdose deaths (contextual evidence review). Previous guidelines have recommended screening or risk assessment tools to identify patients at higher risk for misuse or abuse of opioids. However, the clinical evidence review found that currently available risk-stratification tools (e.g., Opioid Risk Tool, Screener and Opioid Assessment for Patients with Pain Version 1, SOAPP-R, and Brief Risk Interview) show insufficient accuracy for classification of patients as at low or high risk for abuse or misuse (KQ4). Clinicians should always exercise caution when considering or prescribing opioids for any patient with chronic pain outside of active cancer, palliative, and end-of-life care and should not overestimate the ability of these tools to rule out risks from long-term opioid therapy.

Clinicians should ask patients about their drug and alcohol use. Single screening questions can be used (*206*). For example, the question "How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?" (with an answer of one or more considered positive) was found in a primary care setting to be 100% sensitive and 73.5% specific for

the detection of a drug use disorder compared with a standardized diagnostic interview (*207*). Validated screening tools such as the Drug Abuse Screening Test (DAST) (*208*) and the Alcohol Use Disorders Identification Test (AUDIT) (*209*) can also be used. Clinicians should use PDMP data (see Recommendation 9) and drug testing (see Recommendation 10) as appropriate to assess for concurrent substance use that might place patients at higher risk for opioid use disorder and overdose. Clinicians should also provide specific counseling on increased risks for overdose when opioids are combined with other drugs or alcohol (see Recommendation 3) and ensure that patients receive effective treatment for substance use disorders when needed (see Recommendation 12).

The clinical evidence review found insufficient evidence to determine how harms of opioids differ depending on past or current substance use disorder (KQ2), although a history of substance use disorder was associated with misuse. Similarly, based on contextual evidence, patients with drug or alcohol use disorders are likely to experience greater risks for opioid use disorder and overdose than persons without these conditions. If clinicians consider opioid therapy for chronic pain outside of active cancer, palliative, and end-of-life care for patients with drug or alcohol use disorders, they should discuss increased risks for opioid use disorder and overdose with patients, carefully consider whether benefits of opioids outweigh increased risks, and incorporate strategies to mitigate risk into the management plan, such as considering offering naloxone (see Offering Naloxone to Patients When Factors That Increase Risk for Opioid-Related Harms Are Present) and increasing frequency of monitoring (see Recommendation 7) when opioids are prescribed. Because pain management in patients with substance use disorder can be complex, clinicians should consider consulting substance use disorder specialists and pain specialists regarding pain management for persons with active or recent past history of substance abuse. Experts also noted that clinicians should communicate with patients' substance use disorder treatment providers if opioids are prescribed.

Patients with Prior Nonfatal Overdose

Although studies were not identified that directly addressed the risk for overdose among patients with prior nonfatal overdose who are prescribed opioids, based on clinical experience, experts thought that prior nonfatal overdose would substantially increase risk for future nonfatal or fatal opioid overdose. If patients experience nonfatal opioid overdose, clinicians should work with them to reduce opioid dosage and to discontinue opioids when possible (see Recommendation 7). If clinicians continue opioid therapy for chronic pain outside of active cancer, palliative, and end-of-life care in patients with prior opioid overdose, they should discuss increased risks for overdose with patients, carefully consider whether benefits of opioids outweigh substantial risks, and incorporate strategies to mitigate risk into the management plan, such as considering offering naloxone (see

Offering Naloxone to Patients When Factors That Increase Risk for Opioid-Related Harms Are Present) and increasing frequency of monitoring (see Recommendation 7) when opioids are prescribed.

Offering Naloxone to Patients When Factors That Increase Risk for Opioid-Related Harms Are Present

Naloxone is an opioid antagonist that can reverse severe respiratory depression; its administration by lay persons, such as friends and family of persons who experience opioid overdose, can save lives. Naloxone precipitates acute withdrawal among patients physically dependent on opioids. Serious adverse effects, such as pulmonary edema, cardiovascular instability, and seizures, have been reported but are rare at doses consistent with labeled use for opioid overdose (*210*). The contextual evidence review did not find any studies on effectiveness of prescribing naloxone for overdose prevention among patients prescribed opioids for chronic pain. However, there is evidence for effectiveness of naloxone provision in preventing opioid-related overdose death at the community level through community-based distribution (e.g., through overdose education and naloxone distribution programs in community service agencies) to persons at risk for overdose (mostly due to illicit opiate use), and it is plausible that effectiveness would be observed when naloxone is provided in the clinical setting as well. Experts agreed that it is preferable not to initiate opioid treatment when factors that increase risk for opioid-related harms are present. Opinions diverged about the likelihood of naloxone being useful to patients and the circumstances under which it should be offered. However, most experts agreed that clinicians should consider offering naloxone when prescribing opioids to patients at increased risk for overdose, including patients with a history of overdose, patients with a history of substance use disorder, patients taking benzodiazepines with opioids (see Recommendation 11), patients at risk for returning to a high dose to which they are no longer tolerant (e.g., patients recently released from prison), and patients taking higher dosages of opioids (≥50 MME/day). Practices should provide education on overdose prevention and naloxone use to patients receiving naloxone prescriptions and to members of their households. Experts noted that naloxone co-prescribing can be facilitated by clinics or practices with resources to provide naloxone training and by collaborative practice models with pharmacists. Resources for prescribing naloxone in primary care settings can be found through Prescribe to Prevent at http://prescribetoprevent.org.

9. Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid

therapy for chronic pain, ranging from every prescription to every 3 months (recommendation category: A, evidence type: 4).

PDMPs are state-based databases that collect information on controlled prescription drugs dispensed by pharmacies in most states and, in select states, by dispensing physicians as well. In addition, some clinicians employed by the federal government, including some clinicians in the Indian Health Care Delivery System, are not licensed in the states where they practice, and do not have access to PDMP data. Certain states require clinicians to review PDMP data prior to writing each opioid prescription (see state-level PDMP-related policies on the National Alliance for Model State Drug Laws website at http://www.namsdl.org/prescription-monitoring-programs.cfm). The clinical evidence review did not find studies evaluating the effectiveness of PDMPs on outcomes related to overdose, addiction, abuse, or misuse (KQ4). However, even though evidence is limited on the effectiveness of PDMP implementation at the state level on prescribing and mortality outcomes (*28*), the contextual evidence review found that most fatal overdoses were associated with patients receiving opioids from multiple prescribers and/or with patients receiving high total daily opioid dosages; information on both of these risk factors for overdose are available to prescribers in the PDMP. PDMP data also can be helpful when patient medication history is not otherwise available (e.g., for patients from other locales) and when patients transition care to a new clinician. The contextual evidence review also found that PDMP information could be used in a way that is harmful to patients. For example, it has been used to dismiss patients from clinician practices (*211*), which might adversely affect patient safety.

The contextual review found variation in state policies that affect timeliness of PDMP data (and therefore benefits of reviewing PDMP data) as well as time and workload for clinicians in accessing PDMP data. In states that permit delegating access to other members of the health care team, workload for prescribers can be reduced. These differences might result in a different balance of benefits to clinician workload in different states. Experts agreed that PDMPs are useful tools that should be consulted when starting a patient on opioid therapy and periodically during long-term opioid therapy. However, experts disagreed on how frequently clinicians should check the PDMP during long-term opioid therapy, given PDMP access issues and the lag time in reporting in some states. Most experts agreed that PDMP data should be reviewed every 3 months or more frequently during long-term opioid therapy. A minority of experts noted that, given the current burden of accessing PDMP data in some states and the lack of evidence surrounding the most effective interval for PDMP review to improve patient outcomes, annual review of PDMP data during long-term opioid therapy would be reasonable when factors that increase risk for opioid-related harms are not present.

Clinicians should review PDMP data for opioids and other controlled medications patients might have received from additional prescribers to determine whether a patient is receiving high total opioid dosages or dangerous combinations (e.g., opioids combined with benzodiazepines) that put him or her at high risk for overdose. Ideally, PDMP data should be reviewed before every opioid prescription. This is recommended in all states with well-functioning PDMPs and where PDMP access policies make this practicable (e.g., clinician and delegate access permitted), but it is not currently possible in states without functional PDMPs or in those that do not permit certain prescribers to access them. As vendors and practices facilitate integration of PDMP information into regular clinical workflow (e.g., data made available in electronic health records), clinicians' ease of access in reviewing PDMP data is expected to improve. In addition, improved timeliness of PDMP data will improve their value in identifying patient risks.

If patients are found to have high opioid dosages, dangerous combinations of medications, or multiple controlled substance prescriptions written by different clinicians, several actions can be taken to augment clinicians' abilities to improve patient safety:

- Clinicians should discuss information from the PDMP with their patient and confirm that the patient is aware of the additional prescriptions. Occasionally, PDMP information can be incorrect (e.g., if the wrong name or birthdate has been entered, the patient uses a nickname or maiden name, or another person has used the patient's identity to obtain prescriptions).
- Clinicians should discuss safety concerns, including increased risk for respiratory depression and overdose, with patients found to be receiving opioids from more than one prescriber or receiving medications that increase risk when combined with opioids (e.g., benzodiazepines) and consider offering naloxone (see Recommendation 8).
- Clinicians should avoid prescribing opioids and benzodiazepines concurrently whenever possible. Clinicians should communicate with others managing the patient to discuss the patient's needs, prioritize patient goals, weigh risks of concurrent benzodiazepine and opioid exposure, and coordinate care (see Recommendation 11).
- Clinicians should calculate the total MME/day for concurrent opioid prescriptions to help assess the patient's overdose risk (see Recommendation 5). If patients are found to be receiving high total daily dosages of opioids, clinicians should discuss their safety concerns with the patient, consider tapering to a safer dosage (see Recommendations 5 and 7), and consider offering naloxone (see Recommendation 8).
- Clinicians should discuss safety concerns with other clinicians who are prescribing controlled substances for their patient. Ideally clinicians should first discuss concerns with their patient and

inform him or her that they plan to coordinate care with the patient's other prescribers to improve the patient's safety.

- Clinicians should consider the possibility of a substance use disorder and discuss concerns with their patient (see Recommendation 12).
- If clinicians suspect their patient might be sharing or selling opioids and not taking them, clinicians should consider urine drug testing to assist in determining whether opioids can be discontinued without causing withdrawal (see Recommendations 7 and 10). A negative drug test for prescribed opioids might indicate the patient is not taking prescribed opioids, although clinicians should consider other possible reasons for this test result (see Recommendation 10).

Experts agreed that clinicians should not dismiss patients from their practice on the basis of PDMP information. Doing so can adversely affect patient safety, could represent patient abandonment, and could result in missed opportunities to provide potentially lifesaving information (e.g., about risks of opioids and overdose prevention) and interventions (e.g., safer prescriptions, nonopioid pain treatment [see Recommendation 1], naloxone [see Recommendation 8], and effective treatment for substance use disorder [see Recommendation 12]).

10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs (recommendation category: B, evidence type: 4).

Concurrent use of opioid pain medications with other opioid pain medications, benzodiazepines, or heroin can increase patients' risk for overdose. Urine drug tests can provide information about drug use that is not reported by the patient. In addition, urine drug tests can assist clinicians in identifying when patients are not taking opioids prescribed for them, which might in some cases indicate diversion or other clinically important issues such as difficulties with adverse effects. Urine drug tests do not provide accurate information about how much or what dose of opioids or other drugs a patient took. The clinical evidence review did not find studies evaluating the effectiveness of urine drug screening for risk mitigation during opioid prescribing for pain (KQ4). The contextual evidence review found that urine drug testing can provide useful information about patients assumed not to be using unreported drugs. Urine drug testing results can be subject to misinterpretation and might sometimes be associated with practices that might harm patients (e.g., stigmatization, inappropriate termination from care). Routine use of urine drug tests with standardized policies at the practice or clinic level might destigmatize their use. Although random drug testing also might destigmatize urine drug testing, experts thought that truly random testing was not feasible in clinical practice. Some

clinics obtain a urine specimen at every visit, but only send it for testing on a random schedule. Experts noted that in addition to direct costs of urine drug testing, which often are not covered fully by insurance and can be a burden for patients, clinician time is needed to interpret, confirm, and communicate results.

Experts agreed that prior to starting opioids for chronic pain and periodically during opioid therapy, clinicians should use urine drug testing to assess for prescribed opioids as well as other controlled substances and illicit drugs that increase risk for overdose when combined with opioids, including nonprescribed opioids, benzodiazepines, and heroin. There was some difference of opinion among experts as to whether this recommendation should apply to all patients, or whether this recommendation should entail individual decision making with different choices for different patients based on values, preferences, and clinical situations. While experts agreed that clinicians should use urine drug testing before initiating opioid therapy for chronic pain, they disagreed on how frequently urine drug testing should be conducted during long-term opioid therapy. Most experts agreed that urine drug testing at least annually for all patients was reasonable. Some experts noted that this interval might be too long in some cases and too short in others, and that the follow-up interval should be left to the discretion of the clinician. Previous guidelines have recommended more frequent urine drug testing in patients thought to be at higher risk for substance use disorder (*30*). However, experts thought that predicting risk prior to urine drug testing is challenging and that currently available tools do not allow clinicians to reliably identify patients who are at low risk for substance use disorder.

In most situations, initial urine drug testing can be performed with a relatively inexpensive immunoassay panel for commonly prescribed opioids and illicit drugs. Patients prescribed less commonly used opioids might require specific testing for those agents. The use of confirmatory testing adds substantial costs and should be based on the need to detect specific opioids that cannot be identified on standard immunoassays or on the presence of unexpected urine drug test results. Clinicians should be familiar with the drugs included in urine drug testing panels used in their practice and should understand how to interpret results for these drugs. For example, a positive "opiates" immunoassay detects morphine, which might reflect patient use of morphine, codeine, or heroin, but this immunoassay does not detect synthetic opioids (e.g., fentanyl or methadone) and might not detect semisynthetic opioids (e.g., oxycodone). However, many laboratories use an oxycodone immunoassay that detects oxycodone and oxymorphone. In some cases, positive results for specific opioids might reflect metabolites from opioids the patient is taking and might not mean the patient is taking the specific opioid for which the test was positive. For example, hydromorphone

is a metabolite of hydrocodone, and oxymorphone is a metabolite of oxycodone. Detailed guidance on interpretation of urine drug test results, including which tests to order and expected results, drug detection time in urine, drug metabolism, and other considerations has been published previously (*30*). Clinicians should not test for substances for which results would not affect patient management or for which implications for patient management are unclear. For example, experts noted that there might be uncertainty about the clinical implications of a positive urine drug test for tetrahyrdocannabinol (THC). In addition, restricting confirmatory testing to situations and substances for which results can reasonably be expected to affect patient management can reduce costs of urine drug testing, given the substantial costs associated with confirmatory testing methods. Before ordering urine drug testing, clinicians should have a plan for responding to unexpected results. Clinicians should explain to patients that urine drug testing is intended to improve their safety and should also explain expected results (e.g., presence of prescribed medication and absence of drugs, including illicit drugs, not reported by the patient). Clinicians should ask patients about use of prescribed and other drugs and ask whether there might be unexpected results. This will provide an opportunity for patients to provide information about changes in their use of prescribed opioids or other drugs. Clinicians should discuss unexpected results with the local laboratory or toxicologist and with the patient. Discussion with patients prior to specific confirmatory testing can sometimes yield a candid explanation of why a particular substance is present or absent and obviate the need for expensive confirmatory testing on that visit. For example, a patient might explain that the test is negative for prescribed opioids because she felt opioids were no longer helping and discontinued them. If unexpected results are not explained, a confirmatory test using a method selective enough to differentiate specific opioids and metabolites (e.g., gas or liquid chromatography/mass spectrometry) might be warranted to clarify the situation.

Clinicians should use unexpected results to improve patient safety (e.g., change in pain management strategy [see Recommendation 1], tapering or discontinuation of opioids [see Recommendation 7], more frequent re-evaluation [see Recommendation 7], offering naloxone [see Recommendation 8], or referral for treatment for substance use disorder [see Recommendation 12], all as appropriate). If tests for prescribed opioids are repeatedly negative, confirming that the patient is not taking the prescribed opioid, clinicians can discontinue the prescription without a taper. Clinicians should not dismiss patients from care based on a urine drug test result because this could constitute patient abandonment and could have adverse consequences for patient safety, potentially including the patient obtaining opioids from alternative sources and the clinician missing opportunities to facilitate treatment for substance use disorder.

11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible (recommendation category: A, evidence type: 3).

Benzodiazepines and opioids both cause central nervous system depression and can decrease respiratory drive. Concurrent use is likely to put patients at greater risk for potentially fatal overdose. The clinical evidence review did not address risks of benzodiazepine co-prescription among patients prescribed opioids. However, the contextual evidence review found evidence in epidemiologic series of concurrent benzodiazepine use in large proportions of opioid-related overdose deaths, and a case-cohort study found concurrent benzodiazepine prescription with opioid prescription to be associated with a near quadrupling of risk for overdose death compared with opioid prescription alone (*212*). Experts agreed that although there are circumstances when it might be appropriate to prescribe opioids to a patient receiving benzodiazepines (e.g., severe acute pain in a patient taking long-term, stable low-dose benzodiazepine therapy), clinicians should avoid prescribing opioids and benzodiazepines concurrently whenever possible. In addition, given that other central nervous system depressants (e.g., muscle relaxants, hypnotics) can potentiate central nervous system depression associated with opioids, clinicians should consider whether benefits outweigh risks of concurrent use of these drugs. Clinicians should check the PDMP for concurrent controlled medications prescribed by other clinicians (see Recommendation 9) and should consider involving pharmacists and pain specialists as part of the management team when opioids are co-prescribed with other central nervous system depressants. Because of greater risks of benzodiazepine withdrawal relative to opioid withdrawal, and because tapering opioids can be associated with anxiety, when patients receiving both benzodiazepines and opioids require tapering to reduce risk for fatal respiratory depression, it might be safer and more practical to taper opioids first (see Recommendation 7). Clinicians should taper benzodiazepines gradually if discontinued because abrupt withdrawal can be associated with rebound anxiety, hallucinations, seizures, delirium tremens, and, in rare cases, death (contextual evidence review). A commonly used tapering schedule that has been used safely and with moderate success is a reduction of the benzodiazepine dose by 25% every 1–2 weeks (*213*,*214*). CBT increases tapering success rates and might be particularly helpful for patients struggling with a benzodiazepine taper (*213*). If benzodiazepines prescribed for anxiety are tapered or discontinued, or if patients receiving opioids require treatment for anxiety, evidence-based psychotherapies (e.g., CBT) and/or specific anti-depressants or other nonbenzodiazepine medications approved for anxiety should be offered. Experts emphasized that clinicians should communicate with mental health professionals managing the patient to discuss the patient's needs, prioritize patient goals, weigh risks of concurrent benzodiazepine and opioid exposure, and coordinate care.

12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder (recommendation category: A, evidence type: 2).

Opioid use disorder (previously classified as opioid abuse or opioid dependence) is defined in the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5) as a problematic pattern of opioid use leading to clinically significant impairment or distress, manifested by at least two defined criteria occurring within a year (http://pcssmat.org/wp-content/uploads/2014/02/5B-DSM-5-Opioid-Use-Disorder-Diagnostic-Criteria.pdf) (*20*).

The clinical evidence review found prevalence of opioid dependence (using DSM-IV diagnosis criteria) in primary care settings among patients with chronic pain on opioid therapy to be 3%–26% (KQ2). As found in the contextual evidence review and supported by moderate quality evidence, opioid agonist or partial agonist treatment with methadone maintenance therapy or buprenorphine has been shown to be more effective in preventing relapse among patients with opioid use disorder (*151–153*). Some studies suggest that using behavioral therapies in combination with these treatments can reduce opioid misuse and increase retention during maintenance therapy and improve compliance after detoxification (*154,155*); behavioral therapies are also recommended by clinical practice guidelines (*215*). The cited studies primarily evaluated patients with a history of illicit opioid use, rather than prescription opioid use for chronic pain. Recent studies among patients with prescription opioid dependence (based on DSM-IV criteria) have found maintenance therapy with buprenorphine and buprenorphine-naloxone effective in preventing relapse (*216,217*). Treatment need in a community is often not met by capacity to provide buprenorphine or methadone maintenance therapy (*218*), and patient cost can be a barrier to buprenorphine treatment because insurance coverage of buprenorphine for opioid use disorder is often limited (*219*). Oral or long-acting injectable formulations of naltrexone can also be used as medication-assisted treatment for opioid use disorder in nonpregnant adults, particularly for highly motivated persons (*220,221*). Experts agreed that clinicians prescribing opioids should identify treatment resources for opioid use disorder in the community and should work together to ensure sufficient treatment capacity for opioid use disorder at the practice level.

If clinicians suspect opioid use disorder based on patient concerns or behaviors or on findings in prescription drug monitoring program data (see Recommendation 9) or from urine drug testing (see Recommendation 10), they should discuss their concern with their patient and provide an opportunity for the patient to disclose related concerns or problems. Clinicians should assess for the presence of opioid use disorder using DSM-5 criteria (*20*). Alternatively, clinicians can arrange for a

substance use disorder treatment specialist to assess for the presence of opioid use disorder. For patients meeting criteria for opioid use disorder, clinicians should offer or arrange for patients to receive evidence-based treatment, usually medication-assisted treatment with buprenorphine or methadone maintenance therapy in combination with behavioral therapies. Oral or long-acting injectable naltrexone, a long-acting opioid antagonist, can also be used in non-pregnant adults. Naltrexone blocks the effects of opioids if they are used but requires adherence to daily oral therapy or monthly injections. For pregnant women with opioid use disorder, medication-assisted therapy with buprenorphine (without naloxone) or methadone has been associated with improved maternal outcomes and should be offered (see Recommendation 8). Clinicians should also consider offering naloxone for overdose prevention to patients with opioid use disorder (see Recommendation 8). For patients with problematic opioid use that does not meet criteria for opioid use disorder, experts noted that clinicians can offer to taper and discontinue opioids (see Recommendation 7). For patients who choose to but are unable to taper, clinicians may reassess for opioid use disorder and offer opioid agonist therapy if criteria are met.

Physicians not already certified to provide buprenorphine in an office-based setting can undergo training to receive a waiver from the Substance Abuse and Mental Health Services Administration (SAMHSA) that allows them to prescribe buprenorphine to treat patients with opioid use disorder. Physicians prescribing opioids in communities without sufficient treatment capacity for opioid use disorder should strongly consider obtaining this waiver. Information about qualifications and the process to obtain a waiver are available from SAMHSA (*222*). Clinicians do not need a waiver to offer naltrexone for opioid use disorder as part of their practice.

Additional guidance has been published previously (*215*) on induction, use, and monitoring of buprenorphine treatment (see Part 5) and naltrexone treatment (see Part 6) for opioid use disorder and on goals, components of, and types of effective psychosocial treatment that are recommended in conjunction with pharmacological treatment of opioid use disorder (see Part 7). Clinicians unable to provide treatment themselves should arrange for patients with opioid use disorder to receive care from a substance use disorder treatment specialist, such as an office-based buprenorphine or naltrexone treatment provider, or from an opioid treatment program certified by SAMHSA to provide supervised medication-assisted treatment for patients with opioid use disorder. Clinicians should assist patients in finding qualified treatment providers and should arrange for patients to follow up with these providers, as well as arranging for ongoing coordination of care. Clinicians should not dismiss patients from their practice because of a substance use disorder because this can adversely affect patient safety and could represent patient abandonment. Identification of substance use

disorder represents an opportunity for a clinician to initiate potentially life-saving interventions, and it is important for the clinician to collaborate with the patient regarding their safety to increase the likelihood of successful treatment. In addition, although identification of an opioid use disorder can alter the expected benefits and risks of opioid therapy for pain, patients with co-occurring pain and substance use disorder require ongoing pain management that maximizes benefits relative to risks. Clinicians should continue to use nonpharmacologic and nonopioid pharmacologic pain treatments as appropriate (see Recommendation 1) and consider consulting a pain specialist as needed to provide optimal pain management.

Resources to help with arranging for treatment include SAMHSA's buprenorphine physician locator (http://buprenorphine.samhsa.gov/bwns_locator); SAMHSA's Opioid Treatment Program Directory (http://dpt2.samhsa.gov/treatment/directory.aspx); SAMHSA's Provider Clinical Support System for Opioid Therapies (http://pcss-o.org), which offers extensive experience in the treatment of substance use disorders and specifically of opioid use disorder, as well as expertise on the interface of pain and opioid misuse; and SAMHSA's Provider's Clinical Support System for Medication-Assisted Treatment (http://pcssmat.org), which offers expert physician mentors to answer questions about assessment for and treatment of substance use disorders.

Top

Conclusions and Future Directions

Clinical guidelines represent one strategy for improving prescribing practices and health outcomes. Efforts are required to disseminate the guideline and achieve widespread adoption and implementation of the recommendations in clinical settings. CDC will translate this guideline into user-friendly materials for distribution and use by health systems, medical professional societies, insurers, public health departments, health information technology developers, and clinicians and engage in dissemination efforts. CDC has provided a checklist for prescribing opioids for chronic pain (http://stacks.cdc.gov/view/cdc/38025), additional resources such as fact sheets (http://www.cdc.gov/drugoverdose/prescribing/resources.html), and will provide a mobile application to guide clinicians in implementing the recommendations. CDC will also work with partners to support clinician education on pain management options, opioid therapy, and risk mitigation strategies (e.g., urine drug testing). Activities such as development of clinical decision support in electronic health records to assist clinicians' treatment decisions at the point of care; identification of mechanisms that insurers and pharmacy benefit plan managers can use to promote safer prescribing within plans; and development of clinical quality improvement measures and initiatives to improve prescribing and patient care within health systems have promise for increasing guideline

adoption and improving practice. In addition, policy initiatives that address barriers to implementation of the guidelines, such as increasing accessibility of PDMP data within and across states, e-prescribing, and availability of clinicians who can offer medication-assisted treatment for opioid use disorder, are strategies to consider to enhance implementation of the recommended practices. CDC will work with federal partners and payers to evaluate strategies such as payment reform and health care delivery models that could improve patient health and safety. For example, strategies might include strengthened coverage for nonpharmacologic treatments, appropriate urine drug testing, and medication-assisted treatment; reimbursable time for patient counseling; and payment models that improve access to interdisciplinary, coordinated care.

As highlighted in the forthcoming report on the National Pain Strategy, an overarching federal effort that outlines a comprehensive population-level health strategy for addressing pain as a public health problem, clinical guidelines complement other strategies aimed at preventing illnesses and injuries that lead to pain. A draft of the National Pain Strategy has been published previously (*180*). These strategies include strengthening the evidence base for pain prevention and treatment strategies, reducing disparities in pain treatment, improving service delivery and reimbursement, supporting professional education and training, and providing public education. It is important that overall improvements be made in developing the workforce to address pain management in general, in addition to opioid prescribing specifically. This guideline also complements other federal efforts focused on addressing the opioid overdose epidemic including prescriber training and education, improving access to treatment for opioid use disorder, safe storage and disposal programs, utilization management mechanisms, naloxone distribution programs, law enforcement and supply reduction efforts, prescription drug monitoring program improvements, and support for community coalitions and state prevention programs.

This guideline provides recommendations that are based on the best available evidence that was interpreted and informed by expert opinion. The clinical scientific evidence informing the recommendations is low in quality. To inform future guideline development, more research is necessary to fill in critical evidence gaps. The evidence reviews forming the basis of this guideline clearly illustrate that there is much yet to be learned about the effectiveness, safety, and economic efficiency of long-term opioid therapy. As highlighted by an expert panel in a recent workshop sponsored by the National Institutes of Health on the role of opioid pain medications in the treatment of chronic pain, "evidence is insufficient for every clinical decision that a provider needs to make about the use of opioids for chronic pain" (*223*). The National Institutes of Health panel recommended that research is needed to improve our understanding of which types of pain, specific

diseases, and patients are most likely to be associated with benefit and harm from opioid pain medications; evaluate multidisciplinary pain interventions; estimate cost-benefit; develop and validate tools for identification of patient risk and outcomes; assess the effectiveness and harms of opioid pain medications with alternative study designs; and investigate risk identification and mitigation strategies and their effects on patient and public health outcomes. It is also important to obtain data to inform the cost feasibility and cost-effectiveness of recommended actions, such as use of nonpharmacologic therapy and urine drug testing. Research that contributes to safer and more effective pain treatment can be implemented across public health entities and federal agencies (*4*). Additional research can inform the development of future guidelines for special populations that could not be adequately addressed in this guideline, such as children and adolescents, where evidence and guidance is needed but currently lacking. CDC is committed to working with partners to identify the highest priority research areas to build the evidence base. Yet, given that chronic pain is recognized as a significant public health problem, the risks associated with long-term opioid therapy, the availability of effective nonpharmacological and nonopioid pharmacologic treatment options for pain, and the potential for improvement in the quality of health care with the implementation of recommended practices, a guideline for prescribing is warranted with the evidence that is currently available. The balance between the benefits and the risks of long-term opioid therapy for chronic pain based on both clinical and contextual evidence is strong enough to support the issuance of category A recommendations in most cases.

CDC will revisit this guideline as new evidence becomes available to determine when evidence gaps have been sufficiently closed to warrant an update of the guideline. Until this research is conducted, clinical practice guidelines will have to be based on the best available evidence and expert opinion. This guideline is intended to improve communication between clinicians and patients about the risks and benefits of opioid therapy for chronic pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including opioid use disorder, overdose, and death. CDC is committed to evaluating the guideline to identify the impact of the recommendations on clinician and patient outcomes, both intended and unintended, and revising the recommendations in future updates when warranted.

The travel regulations require that "travelers must submit the Travel Expense Reimbursement Voucher with 30 days after completion of their trip". (CAPP Topic 20335, State Travel Regulations, p.7)

In order for the agency to be in compliance with the state travel regulations, please submit your request for today's meeting no later than

February 7, 2017