COURSE #95211 — 3 CONTACT HOURS/CREDITS RELEASE DATE: 09/01/22 EXPIRATION DATE: 08/31/25

Responsible Prescribing of Controlled Substances: The Louisiana Requirement

HOW TO RECEIVE CREDIT

- Read the enclosed course.
- Complete the questions at the end of the course.
- Return your completed Evaluation to NetCE by mail or fax, or complete online at www.NetCE.com. (If you are a physician or Florida nurse, please return the included Answer Sheet/Evaluation.) Your postmark or facsimile date will be used as your completion date.
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Faculty

Mark Rose, BS, MA, LP, is a licensed psychologist in the State of Minnesota with a private consulting practice and a medical research analyst with a biomedical communications firm. Earlier healthcare technology assessment work led to medical device and pharmaceutical sector experience in new product development involving cancer ablative devices and pain therapeutics. Along with substantial experience in addiction research, Mr. Rose has contributed to the authorship of numerous papers on CNS, oncology, and other medical disorders. He is the lead author of papers published in peer-reviewed addiction, psychiatry, and pain medicine journals and has written books on prescription opioids and alcoholism published by the Hazelden Foundation. He also serves as an Expert Advisor and Expert Witness to law firms that represent disability claimants or criminal defendants on cases related to chronic pain, psychiatric/substance use disorders, and acute pharmacologic/toxicologic effects. Mr. Rose is on the Board of Directors of the Minneapolis-based International Institute of Anti-Aging Medicine and is a member of several professional organizations.

Faculty Disclosure

Contributing faculty, Mark Rose, BS, MA, LP, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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The division planners and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience

This course is designed for all Louisiana physicians, osteopaths, physician assistants, and nurses who may alter prescribing practices or intervene to prevent drug diversion and inappropriate controlled substance use.

Accreditations & Approvals

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Special Approvals

This activity is designed to comply with the requirements of California Assembly Bill 1195, Cultural and Linguistic Competency.

This course is approved by the Louisiana State Board Medical Examiners Board to fulfill the requirement for 3 hours of education in drug diversion training, best practices regarding prescribing of controlled substances, and appropriate treatment for addiction.

About the Sponsor

The purpose of NetCE is to provide challenging curricula to assist healthcare professionals to raise their levels of expertise while fulfilling their continuing education requirements, thereby improving the quality of healthcare.

Our contributing faculty members have taken care to ensure that the information and recommendations are accurate and compatible with the standards generally accepted at the time of publication. The publisher disclaims any liability, loss or damage incurred as a consequence, directly or indirectly, of the use and application of any of the contents. Participants are cautioned about the potential risk of using limited knowledge when integrating new techniques into practice.

Disclosure Statement

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Course Objective

The purpose of this course is to provide clinicians who prescribe or distribute opioids with an appreciation for the complexities of opioid prescribing and the dual risks of litigation due to inadequate pain control and drug diversion or misuse in order to provide the best possible patient care and to prevent a growing social problem.

Learning Objectives

Upon completion of this course, you should be able to:

1. Apply epidemiologic trends in opioid use and misuse to current practice so at-risk patient populations can be more easily identified, assessed, and treated.
2. Create comprehensive treatment plans for patients with pain that address patient needs as well as drug diversion prevention.
3. Evaluate behaviors that may indicate drug seeking or diverting as well as approaches for patients suspected of misusing opioids.
4. Identify state and federal laws governing the proper prescription and monitoring of controlled substances.
5. Describe the available treatment modalities for opioid use disorder.

EVIDENCE-BASED PRACTICE RECOMMENDATION

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

Pain is the leading reason for seeking medical care, and pain management is a large part of many healthcare professionals' practice. Opioid analgesics are approved by the U.S. Food and Drug Administration (FDA) for moderate and severe pain and are broadly accepted in acute pain, cancer pain, and end-of-life care, but are controversial in chronic noncancer pain. In response to the long-standing neglect of severe pain, indications for opioid analgesic prescribing were expanded in the 1990s, followed by inappropriate prescribing and increasing abuse, addiction, diversion, and overdose through the 2000s. In tandem with the continued undertreatment of pain, these practice patterns led to needless suffering from uncontrolled pain, opioid analgesic addiction, and overdose. Opioid analgesic prescribing and associated overdose peaked in 2010 with both now in multi-year decline.

Patients show substantial opioid response variations in analgesia and tolerability and may exhibit a range of psychologic, emotional, and behavioral responses that reflect inadequate pain control, an emerging opioid use problem, or both. Clinician delivery of best possible care to patients with pain requires appreciation of the complexities of opioid prescribing and the dual risks of inadequate pain control and inappropriate use, drug diversion, or overdose. A foundation for appropriate opioid prescribing is the understanding of factual data that clarify the prevalence, causality, and prevention of serious safety concerns with opioid prescribing.

SCOPE OF THE PROBLEM

Inappropriate opioid analgesic prescribing for pain is defined as the non-prescribing, inadequate prescribing, excessive prescribing, or continued prescribing despite evidence of ineffectiveness of opioids [1]. Appropriate opioid prescribing is essential to achieve pain control; to minimize patient risk of abuse, addiction, and fatal toxicity; and to minimize societal harms from diversion. The foundation of appropriate opioid prescribing is thorough patient assessment, treatment planning, and follow-up and monitoring. Essential for proper patient assessment and treatment planning is comprehension of the clinical concepts of opioid abuse and addiction, their behavioral manifestations in pain patients, and how these potentially problematic behavioral responses to opioids both resemble and differ from physical dependence and pseudo-dependence. Prescriber knowledge deficit has been identified as a key obstacle to appropriate opioid prescribing and, along with gaps in policy, treatment, attitudes, and research, contributes to widespread inadequate treatment of pain [2].

The current extent of opioid analgesic use in the United States is unprecedented in the country's history and unparalleled anywhere in the world. Before 1990, physicians in the United States were skeptical of prescribing opioids for chronic noncancer pain. But as of 2017, 1 of 25 adults is prescribed an opioid such as oxycodone and hydrocodone for chronic pain, and sales of opioid analgesics now total more than $9 billion each year [3].

Worldwide consumption of opioid analgesics has increased dramatically in the past few decades, with the United States driving a substantial proportion of this increase. For example, the 1990 global consumption of hydrocodone was 4 tons (3,628 kg), compared with the 2020 consumption of 31.2 tons (28,304 kg); 99.2% of this was consumed in the United States [4]. Similarly, 3 tons (2,722 kg) of oxycodone were consumed globally in 1990, versus 64.9 tons (58,876 kg) in 2020, of which 44.3 tons (40,188 kg or 68.2%) were consumed in the United States [4]. With only 4.5% of the world's population, the United States annually consumes more than 80% of all opioid supplies, including [4; 5]:

- 99% of all hydrocodone
- 68% of all oxycodone
- 44% of all methadone
- 47% of all hydromorphone
- 18% of all fentanyl

This disproportionate rate of opioid consumption reflects sociocultural and economic factors and standards of clinical medicine.

Between 1992 and 2003, the U.S. population increased 14%, while persons abusing opioid analgesics increased 94% and first-time non-medical opioid analgesic users 12 to 17 years of age increased 542% [5]. It is interesting to note that while opioid prescribing has increased precipitously among adults in the United States, the rate remained low and steady for children between 1996 and 2012 [6]. To assist in monitoring the public health problem associated with prescribed opioids, numerous governmental, non-profit, and private sector agencies and organizations are involved in collecting, reporting, and analyzing data on the abuse, addiction, fatal overdose, and treatment admissions related to opioid analgesics.

Before it was halted in 2011, the Drug Abuse Warning Network (DAWN) provided estimates of the health consequences of nonmedical use of individual drugs, including opioid medications [7]. DAWN indicates that opioid abuse is a growing problem in the United States. In 2005 and 2011, hydrocodone and its combinations accounted for 51,225 and 97,183 emergency department visits, respectively. Oxycodone and its combinations resulted in 42,810 visits to the emergency department in 2005; this number increased to 175,229 visits in 2011 [8; 9]. Visits for nonmedical use of all opioids increased from 217,594 to 420,040 during the six-year period. According to the Department of Health and Human Services, emergency department visits for opioid overdoses rose 30% in all parts of the United States from July 2016 to September 2017 [10].

Louisiana has been affected by the nonmedical use of prescription drugs and particularly opioid abuse and diversion. In 2017, it ranked 19th in the country in terms of state-wide drug overdose rates [11]. Between 2013 and 2017, Louisiana experienced a 36% increase in drug-related deaths, more than twice the national increase. In addition, the number of overdose deaths from opioids more than doubled between 2012 and 2017 [12]. While deaths involving heroin show a steady increase, deaths involving synthetic opioids (including fentanyl) have rapidly increased. Deaths involving fentanyl have increased by more than 1400% since 2014 [13].

As prescription opioid abuse and unintentional overdose has become a growing concern, more emphasis has been placed on prescribing patterns. In 2017, Louisiana was one of three states (with Tennessee and Mississippi) with the highest rate of short-duration prescriptions filled, each more than 14.0 per 100 persons [14]. In 2017, Louisiana providers wrote 105 opioid prescriptions for every 100 persons, compared to the average U.S. rate of 58.7 prescriptions [15]. In the United States in 2021, Louisiana ranked 24th, with 11% of adults reporting nonmedical use of prescription opioids, compared with its rank of 41st (6.9%) in 2020 [16].

PAIN MANAGEMENT APPROACHES

Healthcare professionals should know the best clinical practices in opioid prescribing, including the associated risks of opioids, approaches to the assessment of pain and function, and pain management modalities. Pharmacologic and nonpharmacologic approaches should be used on the basis of current knowledge in the evidence base or best clinical practices. Patients with moderate-to-severe chronic pain who have been assessed and treated, over a period of time, with non-opioid therapy or nonpharmacologic pain therapy without adequate pain relief, are considered to be candidates for a trial of opioid therapy [17; 18]. Initial treatment should always be considered individually determined and as a trial of therapy, not a definitive course of treatment [19].

In response to a growing need for guidance regarding opioid prescribing practices for chronic pain that also limits diversion and misuse, the Centers for Disease Control and Prevention (CDC) released its guidelines in 2016 [18]. These guidelines include 12 recommendations grouped into three areas: determining when to initiate or continue opioids for chronic pain; opioid selection, dosage, duration, follow-up, and discontinuation; and assessing risk and addressing harms of opioid use (***Table 1***) [18]. The 2016 guidelines communicated the intent to evaluate and reassess evidence and recommendations as new evidence became available. In 2022, the CDC posted a draft of updated guidelines for public comment, based on systematic reviews of new evidence [20; 21; 22]. Release of a final updated guideline is anticipated in late 2022 [20]. Meanwhile, the recommendations referred to in this course are taken from the CDC's 2016 opioid prescribing guideline [18].

In response, the American Academy of Pain Medicine (AAPM) published a consensus panel report evaluating challenges with implementing the CDC guideline [23]. While the AAPM panel generally agreed with the CDC's recommendations, it identified six challenges caused by guideline misapplication [23]:

- Inflexible application of recommended ceiling doses or prescription durations as hard limits
- Abrupt opioid taper or cessation in physically dependent, opioid-treated patients without regard for CDC emphasis on empathically reviewing benefits and risks of continued high-dosage therapy and working collaboratively with patients on a tapering plan
- Lack of availability and coverage for recommended comprehensive, multimodal pain care
- Difficulty of opioid use disorder diagnosis and barriers to accessing evidence-based treatment
- Underutilization of naloxone
- Incomplete data in reporting of overdose death statistics

ACUTE PAIN

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. Acute pain is generally defined as pain lasting less than three months or within the time of normal tissue healing (which could be substantially shorter than three months, depending on the condition) [18].

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 in a quantity no greater than that needed for the expected duration of severe pain. In most cases, three days or less will be sufficient; more than seven days will rarely be needed [18]. However, it is important to note that this guideline is based on emergency department prescribing guidelines for non-traumatic non-surgical pain. It may be necessary to prescribe for longer periods in patients with acute severe pain.

With postoperative, acute, or intermittent pain, analgesia often requires frequent titration, and the two- to four-hour analgesic duration with short-acting hydrocodone, morphine, and oxycodone is more effective than extended-release formulations. Short-acting opioids are also recommended in patients who are medically unstable or with highly variable pain intensity [24; 25; 26].

Clinicians often write prescriptions for long-term use in 30-day increments, and opioid prescriptions written for 30 days or longer are likely to represent initiation or continuation of long-term opioid therapy. Before writing an opioid prescription for 30 days or more, the CDC recommends clinicians should establish treatment goals with patients [18].

CDC RECOMMENDATIONS FOR PRESCRIBING OPIOIDS FOR CHRONIC PAIN OUTSIDE OF ACTIVE CANCER, PALLIATIVE, AND END-OF-LIFE CARE
Determining When to Initiate or Continue Opioids for Chronic Pain
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. 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 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. 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.
Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation
When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids. 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 increasing dosage equal to 50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to equal to 90 MME/day or carefully justify a decision to titrate dosage to equal to 90 MME/day. 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. Clinicians should evaluate benefits and harms with patients within one to four weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every three 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.
Assessing Risk and Addressing Harms of Opioid Use
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 (equal to 50 MME/day), or concurrent benzodiazepine use, are present. 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 three months. 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. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible. 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.
Source: [18] *Table 1*

CHRONIC NON-CANCER PAIN

Chronic non-cancer pain is defined as pain not related to malignancy that lasts one month longer than healing of lesion, that recurs after healing of lesion, that is associated with a non-healing lesion, or that persists for longer than three months [19]. Nonpharmacologic therapy and non-opioid pharmacologic therapy are the preferred first-line therapies for chronic pain. If opioids are used, they should be combined with nonpharmacologic therapy and non-opioid pharmacologic therapy, as appropriate. Clinicians should consider opioid therapy only if expected benefits for pain and function are anticipated to outweigh risks to the patient [18].

Opioid therapy for chronic pain should be presented as a trial for a pre-defined period (e.g., ≤30 days). The goals of treatment should be established with all patients prior to the initiation of opioid therapy, including reasonable improvements in pain, function, depression, anxiety, and avoidance of unnecessary or excessive medication use [1; 18]. The treatment plan should describe therapy selection, measures of progress, and other diagnostic evaluations, consultations, referrals, and therapies.

In opioid-naïve patients, start at the lowest possible dose and titrate to effect. Dosages for opioid-tolerant patients should always be individualized and titrated by efficacy and tolerability [1; 18]. When starting opioid therapy for chronic pain, clinicians should prescribe short-acting instead of extended-release/long-acting opioid formulations [18].

The need for frequent progress and benefit/risk assessments during the trial should be included in patient education. Patients should also have full knowledge of the warning signs and symptoms of respiratory depression. Prescribers should carefully reassess evidence of benefits and risks when increasing the dosage to ≥ 50 mg morphine equivalent dose (MED) per day. Decisions to titrate dose to ≥ 90 mg MED/day should be avoided or carefully justified [18].

Prescribers should be knowledgeable of federal and state opioid prescribing regulations. Issues of equianalgesic dosing, close patient monitoring during all dose changes, and cross-tolerance with opioid conversion should be considered. If necessary, treatment may be augmented, with preference for nonopioid and immediate-release opioids over long-acting/extended-release opioids. Taper opioid dose when no longer needed [27].

PALLIATIVE CARE AND PAIN AT THE END OF LIFE

Unrelieved pain is the greatest fear among people with a life-limiting disease, and the need for an increased understanding of effective pain management is well-documented [28]. Although experts have noted that 75% to 90% of end-of-life pain can be managed effectively, rates of pain are high, even among people receiving palliative care [28; 29; 30; 31; 32; 33; 34; 35; 36; 37].

The inadequate management of pain is the result of several factors related to both patients and clinicians. In a survey of oncologists, patient reluctance to take opioids or to report pain were two of the most important barriers to effective pain relief [38]. This reluctance is related to a variety of attitudes and beliefs [28; 38]:

- Fear of addiction to opioids
- Worry that if pain is treated early, there will be no options for treatment of future pain
- Anxiety about unpleasant side effects from pain medications
- Fear that increasing pain means that the disease is getting worse
- Desire to be a "good" patient
- Concern about the high cost of medications

Education and open communication are the keys to overcoming these barriers. Every member of the healthcare team should reinforce accurate information about pain management with patients and families. The clinician should initiate conversations about pain management, especially regarding the use of opioids, as few patients will raise the issue themselves or even express their concerns unless they are specifically asked [39]. It is important to acknowledge patients' fears individually and provide information to help them differentiate fact from fiction. For example, when discussing opioids with a patient who fears addiction, the clinician should explain that the risk of addiction is low [28]. It is also helpful to note the difference between addiction and physical dependence.

There are several other ways clinicians can allay patients' fears about pain medication:

- Assure patients that the availability of pain relievers cannot be exhausted; there will always be medications if pain becomes more severe.
- Acknowledge that side effects may occur but emphasize that they can be managed promptly and safely and that some side effects will abate over time.
- Explain that pain and severity of disease are not necessarily related.

Encouraging patients to be honest about pain and other symptoms is also vital. Clinicians should ensure that patients understand that pain is multidimensional and emphasize the importance of talking to a member of the healthcare team about possible causes of pain, such as emotional or spiritual distress. The healthcare team and patient should explore psychosocial and cultural factors that may affect self-reporting of pain, such as concern about the cost of medication.

Clinicians' attitudes, beliefs, and experiences also influence pain management, with addiction, tolerance, side effects, and regulations being the most important concerns [28; 35; 38; 40; 41; 42]. A lack of appropriate education and training in the assessment and management of pain has been noted to be a substantial contributor to ineffective pain management [38; 40; 42; 43]. As a result, many clinicians, especially primary care physicians, do not feel confident about their ability to manage pain in their patients [38; 40].

Clinicians require a clear understanding of available medications to relieve pain, including appropriate dosing, safety profiles, and side effects. If necessary, clinicians should consult with pain specialists to develop an effective approach.

ASSESSMENT OF PAIN

Pain should be assessed routinely, and frequent assessment has become the standard of care [44]. Pain is a subjective experience, and as such, the patient's self-report of pain is the most reliable indicator. Research has shown that pain is underestimated by healthcare professionals and overestimated by family members [44; 45]. Therefore, it is essential to obtain a pain history directly from the patient, when possible, as a first step toward determining the cause of the pain and selecting appropriate treatment strategies. When the patient is unable to communicate verbally, other strategies must be used to determine the characteristics of the pain.

Questions should be asked to elicit descriptions of the pain characteristics, including its location, distribution, quality, temporal aspect, and intensity. In addition, the patient should be asked about aggravating or alleviating factors. Pain is often felt in more than one area, and physicians should attempt to discern if the pain is focal, multifocal, or generalized. Focal or multifocal pain usually indicates an underlying tissue injury or lesion, whereas generalized pain could be associated with damage to the central nervous system. Pain can also be referred, usually an indicator of visceral pain.

The quality of the pain refers to the sensation experienced by the patient, and it often suggests the pathophysiology of the pain [44]. Pain that is well localized and described as aching, throbbing, sharp, or pressure-like is most likely somatic nociceptive pain. This type of pain is usually related to damage to bones and soft tissues. Diffuse pain that is described as squeezing, cramping, or gnawing is usually visceral nociceptive pain. Pain that is described as burning, tingling, shooting, or shock-like is neuropathic pain, which is generally a result of a lesion affecting the nervous system.

Documentation of pain intensity is key, as several treatment decisions depend on the intensity of the pain. The numeric rating scale is the tool used most often to assess pain; with this tool, patients rate pain on a scale of 0 to 10 [44]. Functional assessment is also important. The healthcare team should observe the patient to see how pain limits movements and should ask the patient or family how the pain interferes with normal activities. Determining functional limitations can help enhance patient compliance in reporting pain and adhering to pain-relieving measures, as clinicians can discuss compliance in terms of achieving established functional goals [39]. The Memorial Pain Assessment Card can be used to evaluate both the severity of pain and the effect of pain on function [44; 46].

Physical examination can be valuable in determining an underlying cause of pain. Examination of painful areas can detect evidence of trauma, skin breakdown, or changes in osseous structures. Auscultation can detect abnormal breath or bowel sounds; percussion can detect fluid accumulation; and palpation can reveal tenderness. A neurologic examination should also be carried out to evaluate sensory and/or motor loss and changes in reflexes. During the examination, the clinician should watch closely for nonverbal cues that suggest pain, such as moaning, grimacing, and protective movements. These cues are especially important when examining patients who are unable to verbally communicate about pain.

CREATING A TREATMENT PLAN AND ASSESSMENT OF ADDICTION RISK

Nonpharmacologic therapy and non-opioid pharmacologic therapy are preferred for chronic pain [18]. Clinicians should consider opioid therapy only if expected benefits for pain and function are anticipated to outweigh risks to the patient. Pharmacologic and nonpharmacologic approaches should be used on the basis of current knowledge in the evidence base or best clinical practices. Patients with moderate-to-severe chronic pain who have been assessed and treated, over a period of time, with non-opioid pharmacologic or nonpharmacologic pain therapy without adequate pain relief are considered to be candidates for a trial of opioid therapy. The treatment plan should always be individualized for the patient and begun as a trial for a defined period of time (usually no more than 30 days) before embarking on a definitive course of treatment [1].

If opioids are used, they should be combined with nonpharmacologic therapy and non-opioid pharmacologic therapy, as appropriate. Before starting opioid therapy for chronic pain, clinicians should, for all patients:

- Establish treatment goals for pain and function.
- Consider how therapy will be discontinued if benefits do not outweigh risks.
- Continue opioid therapy only if clinically meaningful improvement in pain and function outweighs safety risks.

Several nonpharmacologic approaches are therapeutic complements to pain-relieving medication, lessening the need for higher doses and perhaps minimizing side effects. These interventions can help decrease pain or distress that may be contributing to the pain sensation. Approaches include palliative radiotherapy, complementary/alternative methods, manipulative and body-based methods, and cognitive/behavioral techniques. The choice of a specific nonpharmacologic intervention is based on the patient's preference, which, in turn, is usually based on a successful experience in the past.

Multidisciplinary functional restoration programs, which are intensive (>100 hours) biopsychosocial interventions whereby physical rehabilitation is combined with cognitive-behavioral therapy and delivered by an interdisciplinary team, embody this recommendation. Moderate-to-strong evidence supports their efficacy in chronic pain. They have been found effective in reducing pain and improving physical function, work readiness, and return to work. Weaker outcomes are found in programs that are less intensive or lacking a behavioral component. Patients who do not improve with less intensive therapy options and have high levels of pain, distress, and disability should be considered for multidisciplinary functional restoration programs [47].

Nonopioid analgesics, such as aspirin, acetaminophen, and nonsteroidal anti-inflammatory drugs (NSAIDs), are primarily used for mild pain and may also be helpful as coanalgesics for patients with moderate or severe pain. Acetaminophen is among the safest of analgesic agents, but it has essentially no anti-inflammatory effect. Toxicity is a concern at high doses, and the maximum recommended dose is 3–4 g per day [44]. Acetaminophen should be avoided or given at lower doses in people with a history of alcohol abuse or renal or hepatic insufficiency [44].

NSAIDs are most effective for pain associated with inflammation. Among the commonly used NSAIDs are ibuprofen, naproxen, and indomethacin. There are several classes of NSAIDs, and the response differs among patients; trials of drugs for an individual patient may be necessary to determine which drug is most effective [48]. NSAIDs inhibit platelet aggregation, increasing the risk of bleeding, and also can damage the mucosal lining of the stomach, leading to gastrointestinal bleeding. There is a ceiling effect to the nonopioid analgesics; that is, there is a dose beyond which there is no further analgesic effect. In addition, many side effects of nonopioids can be severe and may limit their use or dosing.

Moderate pain has often been treated with analgesic agents that are combinations of acetaminophen and an opioid, such as codeine, oxycodone, or hydrocodone. However, it is now recommended that these combination drugs be avoided, as limits on the maximum dose of acetaminophen limits the use of a combination drug [44; 49]. Individual drugs in combination are preferred, allowing for increases in the dose of the opioid without increasing the dose of the coanalgesic.

Strong opioids are used for severe pain [31; 44; 50; 51]. Unlike nonopioids, opioids do not have a ceiling effect, and the dose can be titrated until pain is relieved or side effects become unmanageable.

Information obtained by patient history, physical examination, and interview, from family members, a spouse, or state prescription drug monitoring program (PDMP), and from the use of screening and assessment tools can help the clinician to stratify the patient according to level of risk for developing problematic opioid behavioral responses (***Table 2***). Low-risk patients receive the standard level of monitoring, vigilance, and care. Moderate-risk patients should be considered for an additional level of monitoring and provider contact, and high-risk patients are likely to require intensive and structured monitoring and follow-up contact, additional consultation with psychiatric and addiction medicine specialists, and limited supplies of short-acting opioid formulations [18; 52].

A simplified approach to opioid prescribing safety, based on the core concept of universal precautions but designed with high specificity for opioid analgesics, was presented at the 2013 annual conference of the AAPM. The eight principles are specifically intended to reduce fatalities with opioid analgesic prescribing and are now incorporated in the AAPM Safe Opioid Prescribing Initiative [54]. They may be recalled using the acronym RELIABLE:

- **R**espiratory: If a patient on long-term opioids develops a respiratory condition (e.g., asthma, pneumonia, flu), reduce the opioid dose by 20% to 30%.

RISK STRATIFICATION FOR PATIENTS PRESCRIBED OPIOIDS
Low Risk
Definable physical pathology with objective signs and reliable symptoms
Clinical correlation with diagnostic testing, including MRI, physical examination, and interventional diagnostic techniques
With or without mild psychologic comorbidity
With or without minor medical comorbidity
No or well-defined and controlled personal or family history of alcoholism or substance abuse
Age 45 years or older
High levels of pain acceptance and active coping strategies
High motivation and willingness to participate in multimodal therapy and attempting to function at normal levels
Medium Risk
Significant pain problems with objective signs and symptoms confirmed by radiologic evaluation, physical examination, or diagnostic interventions
Moderate psychologic problems, well controlled by therapy
Moderate coexisting medical disorders that are well controlled by medical therapy and are not affected by chronic opioid therapy (e.g., central sleep apnea)
Develops mild tolerance but not hyperalgesia without physical dependence or addiction
Past history of personal or family history of alcoholism or substance abuse
Pain involving more than three regions of the body
Defined pathology with moderate levels of pain acceptance and coping strategies
Willing to participate in multimodal therapy, attempting to function in normal daily life
High Risk
Widespread pain without objective signs and symptoms
Pain involving more than three regions of the body
Aberrant drug-related behavior
History of alcoholism or drug misuse, abuse, addiction, diversion, dependency, tolerance, or hyperalgesia
Major psychologic disorders
Age younger than 45 years
HIV-related pain
High levels of pain exacerbation and low levels of coping strategies
Unwilling to participate in multimodal therapy, not functioning close to a near normal lifestyle
HIV = human immunodeficiency syndrome, MRI = magnetic resonance imaging.
Source: [53] *Table 2*

- **E**xperience: Assess the patient before prescribing opioids to explore biologic, social, and psychiatric risk factors.
- **L**ong-term: Extended-release opioids should not be used for acute pain.
- **I**nitiating methadone: Never start methadone at a dose ≥15 mg/day.
- **A**pnea: Screen for hypoxemia and obstructive or central sleep apnea, especially in patients who are taking 150 mg/day MED or who are obese, infirm, or elderly.
- **B**enzodiazepines: Avoid these agents if possible because they enhance opioid toxicity.

- Look for comorbidities: Patients often misuse opioid analgesics for their mental health disorder instead of their pain, so assess patients for a history of bipolar disorder, post-traumatic stress disorder, depression, stress, and general anxiety disorder.
- Exercise caution with rotation: Conversion tables and equal analgesic tables should not be used to determine opioid starting doses. Assume everyone is opioid naïve, start on a low dose, and titrate slowly to the maximum dose one can safely prescribe.

Before deciding to prescribe an opioid analgesic, clinicians should perform and document a detailed patient assessment that includes [1]:

- Pain indications for opioid therapy
- Nature and intensity of pain
- Past and current pain treatments and patient response
- Comorbid conditions
- Pain impact on physical and psychologic function
- Social support, housing, and employment
- Home environment (i.e., stressful or supportive)
- Pain impact on sleep, mood, work, relationships, leisure, and substance use
- Patient history of physical, emotional, or sexual abuse

If substance abuse is active, in remission, or in the patient's history, consult an addiction specialist before starting opioids [1]. In active substance abuse, do not prescribe opioids until the patient is engaged in treatment/recovery program or other arrangement made, such as addiction professional co-management and additional monitoring. When considering an opioid analgesic (particularly those that are extended-release or long-acting), one must always weigh the benefits against the risks of overdose, abuse, addiction, physical dependence and tolerance, adverse drug interactions, and accidental exposure by children [18; 27].

According to the American Society of Interventional Pain Physicians, before starting opioid therapy, clinicians must take certain basic steps to prevent opioid abuse: distinguish individual opioid abuse risk factors; screen patients' potential for addiction and abuse during their initial visit; categorize patients in accordance with their level of risk and implement an appropriate level of monitoring; and refrain from judgments before a thorough assessment. Combining the above strategies with point-of-care urine drug testing as a confirmatory tool have been shown to contribute significantly to the identification of inconsistencies.

(https://www.painphysicianjournal.com/current/pdf?article=NDIwNA%3D%3D&journal=103. Last accessed August 25, 2022.)

Level of Evidence: Expert Opinion/Consensus Statement

RISK ASSESSMENT TOOLS

Screening and assessment tools can help guide patient stratification according to risk level and inform the appropriate degree of structure and monitoring in the treatment plan. It should be noted that despite widespread endorsement of screening tool use to help determine patient risk level, most tools have not been extensively evaluated, validated, or compared to each other, and evidence of their reliability is poor [53].

Opioid Risk Tool (ORT)

The Opioid Risk Tool (ORT) is a five-item assessment to help predict aberrant drug-related behavior. The ORT is also used to establish patient risk level through categorization into low, medium, or high levels of risk for aberrant drug-related behaviors based on responses to questions of previous alcohol/drug abuse, psychologic disorders, and other risk factors [55; 56].

Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R)

The Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R) is a patient-administered, 24-item screen with questions addressing history of alcohol/substance use, psychologic

status, mood, cravings, and stress. Like the ORT, the SOAPP-R helps assess risk level of aberrant drug-related behaviors and the appropriate extent of monitoring [57; 58].

CAGE and CAGE-AID

The original CAGE (Cut down, Annoyed, Guilty, and Eye-opener) Questionnaire consisted of four questions designed to help clinicians determine the likelihood that a patient was misusing or abusing alcohol. These same four questions were modified to create the CAGE-AID (adapted to include drugs), revised to assess the likelihood of current substance abuse [59; 60].

Diagnosis, Intractability, Risk, and Efficacy (DIRE) Tool

The Diagnosis, Intractability, Risk, and Efficacy (DIRE) risk assessment tool is a clinician-rated questionnaire that is used to predict patient compliance with long-term opioid therapy [61; 62]. Patients scoring lower on the DIRE tool are poor candidates for long-term opioid analgesia.

Mental Health Screening Tool

The Mental Health Screening Tool is a five-item screen that asks about a patient's feelings of happiness, calmness, peacefulness, nervousness, and depression in the past month [63]. A lower score on this tool is an indicator that the patient should be referred to a specialist for pain management.

Informed Consent and Treatment Agreements

The initial opioid prescription is preceded by a written informed consent or "treatment agreement" [1]. This agreement should address potential side effects, tolerance and/or physical dependence, drug interactions, motor skill impairment, limited evidence of long-term benefit, misuse, dependence, addiction, and overdose. Informed consent documents should include information regarding the risk/benefit profile for the drug(s) being prescribed. The prescribing policies should be clearly delineated, including the number/frequency of refills, early refills, and procedures for lost or stolen medications.

The treatment agreement also outlines joint physician and patient responsibilities. The patient agrees to using medications safely, refraining from "doctor shopping," and consenting to routine urine drug testing (UDT). The prescriber's responsibility is to address unforeseen problems and prescribe scheduled refills. Reasons for opioid therapy change or discontinuation should be listed. Common components of an opioid treatment agreement include [64]:

- Timeframe of the agreement
- Goals of therapy
- Risks and benefits of chronic opioid therapy
- Requirement for obtaining prescriptions from a single clinician and a named pharmacy
- Activities for pain management
- Risk and benefit statement, including lists of possible side effects
- Proscription against changing medication dosage without permission
- Schedule for regular medical visits for evaluation of the agreed-on treatment
- Requirement of complete, honest self-report of pain relief, side effects, and function at each medical visit
- Limits on medication refills
- Limits on replacing lost medications or prescriptions
- Consent for random UDT and other specified testing
- Required pill counts
- Consent for appropriate release of information (e.g., from family members, other clinicians, counselors, substance abuse treatment programs)
- Requirements of the clinician
- Participation in agreed-on psychiatric treatment activities
- Possible consequences of not following the treatment agreement

A treatment agreement can be used to clearly delineate treatment boundaries and reinforce adherence to medication routines and to nonpharmacologic therapies [1]. Significant deviation from a treatment agreement may indicate that consultation with other healthcare providers or transfer of the patient's care to a specialist is warranted. Any actions the patient is expected to take to return to adherence should be clearly explained [64].

PERIODIC REVIEW AND MONITORING

When implementing a chronic pain treatment plan that involves the use of opioids, the patient should be frequently reassessed for changes in pain origin, health, and function [1]. This can include input from family members and/or the state PDMP. During the initiation phase and during any changes to the dosage or agent used, patient contact should be increased. At every visit, chronic opioid response may be monitored according to the "5 A's" [1; 65]:

- Analgesia
- Activities of daily living
- Adverse or side effects
- Aberrant drug-related behaviors
- Affect (i.e., patient mood)

Signs and symptoms that, if present, may suggest a problematic response to the opioid and interference with the goal of functional improvement include [66]:

- Excessive sleeping or days and nights turned around
- Diminished appetite
- Short attention span or inability to concentrate
- Mood volatility, especially irritability
- Lack of involvement with others
- Impaired functioning due to drug effects
- Use of the opioid to regress instead of re-engaging in life
- Lack of attention to hygiene and appearance

The decision to continue, change, or terminate opioid therapy is based on progress toward treatment objectives and absence of adverse effects and risks of overdose or diversion [1]. Satisfactory therapy is indicated by improvements in pain, function, and quality of life. Brief assessment tools to assess pain and function may be useful, as may UDTs. Treatment plans may include periodic pill counts to confirm adherence and minimize diversion.

Involvement of Family

Family members of the patient can provide the clinician with valuable information that better informs decision making regarding continuing opioid therapy. Family members can observe whether a patient is losing control of his or her life or becoming less functional or more depressed during the course of opioid therapy. They can also provide input regarding positive or negative changes in patient function, attitude, and level of comfort. The following questions can be asked of family members or a spouse to help clarify whether the patient's response to opioid therapy is favorable or unfavorable [66]:

- Is the person's day centered around taking the opioid medication? Response can help clarify long-term risks and benefits of the medication and identify other treatment options.
- Does the person take pain medication only on occasion, perhaps three or four times per week? If yes, the likelihood of addiction is low.
- Have there been any other substance (alcohol or drug) abuse problems in the person's life? An affirmative response should be taken into consideration when prescribing.
- Does the person in pain spend most of the day resting, avoiding activity, or feeling depressed? If so, this suggests the pain medication is failing to promote rehabilitation. Daily activity is essential, and the patient may be considered for enrollment in a graduated exercise program

- Is the person in pain able to function (e.g., work, do household chores, play) with pain medication in a way that is clearly better than without? If yes, this suggests the pain medication is contributing to wellness.

Assessment Tools

VIGIL

VIGIL is the acronym for a five-step risk management strategy designed to empower clinicians to appropriately prescribe opioids for pain by reducing regulatory concerns and to give pharmacists a framework for resolving ambiguous opioid analgesic prescriptions in a manner that preserves legitimate patient need while potentially deterring diverters. The components of VIGIL are:

- Verification: Is this a responsible opioid user?
- Identification: Is the identity of this patient verifiable?
- Generalization: Do we agree on mutual responsibilities and expectations?
- Interpretation: Do I feel comfortable allowing this person to have controlled substances?
- Legalization: Am I acting legally and responsibly?

The foundation of VIGIL is a collaborative physician/pharmacist relationship [67].

Current Opioid Misuse Measure (COMM)

The Current Opioid Misuse Measure (COMM) is a 17-item patient self-report assessment designed to help clinicians identify misuse or abuse in chronic pain patients. Unlike the ORT and the SOAPP-R, the COMM identifies aberrant behaviors associated with opioid misuse in patients already receiving long-term opioid therapy [52]. Sample questions include: In the past 30 days, how often have you had to take more of your medication than prescribed? In the past 30 days, how much of your time was spent thinking about opioid medications (e.g., having enough, taking them, dosing schedule)?

Pain Assessment and Documentation Tool (PADT)

Guidelines by the CDC, the Federation of State Medical Boards (FSMB), and the Joint Commission stress the importance of documentation from both a healthcare quality and medicolegal perspective. Research has found widespread deficits in chart notes and progress documentation with chronic pain patients receiving opioid therapy, and the Pain Assessment and Documentation Tool (PADT) was designed to address these shortcomings [68]. The PADT is a clinician-directed interview, with most sections (e.g., analgesia, activities of daily living, adverse events) consisting of questions asked of the patient. However, the potential aberrant drug-related behavior section must be completed by the physician based on his or her observations of the patient.

The Brief Intervention Tool

The Brief Intervention Tool is a 26-item, "yes-no," patient-administered questionnaire used to identify early signs of opioid abuse or addiction. The items assess the extent of problems related to drug use in several areas, including drug use-related functional impairment [63].

Urine Drug Tests

UDTs may be used to monitor adherence to the prescribed treatment plan and to detect unsanctioned drug use. Noncompliance to an opioid treatment plan is a risk factor for misuse and diversion and should be considered when deciding whether or not to continue therapy. UDTs should be used more often in patients receiving addiction therapy, but clinical judgment is the ultimate guide to testing frequency (***Table 3***) [69]. The CDC recommends clinicians should use UDT before starting opioid therapy and consider UDT at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs [18]. However, this recommendation was based on low-quality evidence that indicates little confidence in the effect estimate.

PATIENT RISK LEVEL AND FREQUENCY OF MONITORING			
	Patient Risk Level		
Monitoring Tool	Low	Medium	High
Urine drug test	Every 1 to 2 years	Every 6 to 12 months	Every 3 to 6 months
State prescription drug monitoring program	Twice per year	Three times per year	Four times per year

Source: [69] *Table 3*

Initially, testing involves the use of class-specific immunoassay drug panels [1]. If necessary, this may be followed with gas chromatography/mass spectrometry for specific drug or metabolite detection. It is important that testing identifies the specific drug rather than the drug class, and the prescribed opioid should be included in the screen. Any abnormalities should be confirmed with a laboratory toxicologist or clinical pathologist. Immunoassay may be used point-of-care for "on-the-spot" therapy changes, but the high error rate prevents its use in major clinical decisions except with liquid chromatography coupled to tandem mass spectrometry confirmation.

Urine test results suggesting opioid misuse should be discussed with the patient using a positive, supportive approach. The test results and the patient discussion should be documented.

CONSULTATION AND REFERRAL

It is important to seek consultation or patient referral when input or care from a pain, psychiatry, addiction, or mental health specialist is necessary. Clinicians who prescribe opioids should become familiar with opioid addiction treatment options (including licensed opioid treatment programs for methadone and office-based opioid treatment for buprenorphine) if referral is needed [1].

Ideally, providers should be able to refer patients with active substance abuse who require pain treatment to an addiction professional or specialized program. In reality, these specialized resources are scarce or non-existent in many areas [1]. Therefore, each provider will need to decide whether the risks of continuing opioid treatment while a patient is using illicit drugs outweigh the benefits to the patient in terms of pain control and improved function [70].

DOCUMENTATION

As noted, documentation is a necessary aspect of all patient care, but it is of particular importance when opioid prescribing is involved. All clinicians should maintain accurate, complete, and up-to-date medical records, including all written or telephoned prescription orders for opioid analgesics and other controlled substances, all written instructions to the patient for medication use, and the name, telephone number, and address of the patient's pharmacy [1]. Good medical records demonstrate that a service was provided to the patient and that the service was medically necessary. Regardless of the treatment outcome, thorough medical records protect the prescriber.

When documenting an opioid treatment plan, the first step is adherence to state and federal laws pertaining to the prescription of controlled substance prescribing. A prescription for a controlled substance must include the following information [71; 72]:

- Date of issue
- Patient's name and address
- Practitioner's name, address, and DEA registration number
- Drug name
- Drug strength
- Dosage form
- Quantity prescribed
- Directions for use
- Number of refills (if any) authorized (schedule II drugs may not be refilled)
- Manual signature of prescriber

In emergency situations, a prescription for a schedule II controlled substance may be telephoned to the pharmacy and the prescriber must follow up with a written prescription being sent to the pharmacy within seven days [73].

Follow-up visits and screening should also be clearly and completely documented. At a minimum, the frequency of visits, exams, screens, contact (e.g., e-mail, phone calls), and prescriptions without visits should be documented [74]. Previous plans and outcomes should be reviewed with the patient and documented in his or her record. Ongoing screening and assessments (e.g., UDTs, 5A's) should be recorded. Some experts recommend that each medical record have a dedicated page or section to list all of the patient's current medications (including dosages, fill dates, and refills) and that this list be updated at each patient visit [74].

PATIENT EDUCATION ON THE USE AND DISPOSAL OF OPIOIDS

Patients and caregivers should be counseled regarding the safe use and disposal of opioids. As part of its mandatory Risk Evaluation and Mitigation Strategy (REMS) for extended-release/long-acting opioids, the U.S. Food and Drug Administration (FDA) has developed a patient counseling document with information on the patient's specific medications, instructions for emergency situations and incomplete pain control, and warnings not to share medications or take them unprescribed [27]. A copy of this form may be accessed online at https://www.fda.gov/media/86281/download.

When prescribing opioids, clinicians should provide patients with the following information [27]:

- Product-specific information
- Taking the opioid as prescribed
- Importance of dosing regimen adherence, managing missed doses, and prescriber contact if pain is not controlled
- Warning and rationale to never break or chew/crush tablets or cut or tear patches prior to use
- Warning and rationale to avoid other central nervous system depressants, such as sedative-hypnotics, anxiolytics, alcohol, or illicit drugs
- Warning not to abruptly halt or reduce the opioid without physician oversight of safe tapering when discontinuing
- The potential of serious side effects or death
- Risk factors, signs, and symptoms of overdose and opioid-induced respiratory depression, gastrointestinal obstruction, and allergic reactions
- The risks of falls, using heavy machinery, and driving
- Warning and rationale to never share an opioid analgesic
- Rationale for secure opioid storage
- Warning to protect opioids from theft
- Instructions for disposal of unneeded opioids, based on product-specific disposal information

There are no universal recommendations for the proper disposal of unused opioids, and patients are rarely advised of what to do with unused or expired medications [75]. According to the Office of National Drug Control Policy, most medications that are no longer necessary or have expired should be removed from their containers, mixed with undesirable substances (e.g., cat litter, used coffee grounds), and put into an impermeable, nondescript container (e.g., disposable container with a lid or a sealed bag) before throwing in the trash [76]. Any personal information should be obscured or destroyed. The FDA recommends that certain medications, including oxycodone/acetaminophen (Percocet), oxycodone (OxyContin tablets), and transdermal fentanyl (Duragesic Transdermal System), be flushed down the toilet instead of thrown in the trash [76]. Patients should be advised to flush prescription drugs down the toilet only if the label or accompanying patient information specifically instructs doing so.

The American College of Preventive Medicine has established best practices to avoid diversion of unused drugs and educate patients regarding drug disposal [75]:

- Consider writing prescriptions in smaller amounts.
- Educate patients about safe storing and disposal practices.
- Give drug-specific information to patients about the temperature at which they should store their medications. Generally, the bathroom is not the best storage place. It is damp and moist, potentially resulting in potency decrements, and accessible to many people, including children and teens, resulting in potential theft or safety issues.
- Ask patients not to advertise that they are taking these types of medications and to keep their medications secure.
- Refer patients to community "take back" services overseen by law enforcement that collect controlled substances, seal them in plastic bags, and store them in a secure location until they can be incinerated. Contact your state law enforcement agency or visit https://www.dea.gov to determine if a program is available in your area.

TAPERING AND DISCONTINUING OPIOID THERAPY

The decision to continue or end opioid prescribing should be based on a physician-patient discussion of the anticipated benefits and risks. An opioid should be discontinued with resolution of the pain condition, intolerable side effects, inadequate analgesia, lack of improvement in quality of life despite dose titration, deteriorating function, or significant aberrant medication use [1; 18].

Clinicians should provide physically dependent patients with a safely structured tapering protocol. Withdrawal is managed by the prescribing physician or referral to an addiction specialist. Patients should be reassured that opioid discontinuation is not the end of treatment; continuation of pain management will be undertaken with other modalities through direct care or referral.

As a side note, cannabis use by chronic pain patients receiving opioid therapy has traditionally been viewed as a treatment agreement violation that is grounds for termination of opioid therapy. However, some now argue against cannabis use as a rationale for termination or substantial treatment and monitoring changes, especially considering the increasing legalization of medical use at the state level [70].

POLYPHARMACY AND MEDICATION RECONCILIATION

The term polypharmacy is often used but not well defined. There are varied definitions in medical literature, but in general, polypharmacy has been defined as a single patient taking more than 5 drugs every day, with excessive polypharmacy defined as the prescription of 10 or more daily medications [77; 78]. Polypharmacy may be used to describe excessive or unnecessary medications, inappropriate prescribing, or excessive use, overuse, or duplication of medications. There has been a call to redefine polypharmacy beyond an arbitrary number of medications [78; 79]. In some cases of multimorbidity and chronic conditions (e.g., hypertension), the use of multiple medications may be the best practice according to clinical guidelines; this may be referred to as "appropriate polypharmacy" [80]. However, even when the prescription of multiple medications is warranted, it raises the risks of drug interactions, compliance issues, and adverse effects. Generally, the term polypharmacy has a negative connotation and is associated with the co-prescribing of potentially inappropriate medications.

Medication reconciliation is the process of creating and updating a current medication list as compared with any previous lists. This should be conducted:

- On admission
- During routine and acute visits by providers
- After transitions of care
- During significant change in condition
- When the goals of care change
- Before prescribing new medications
- When discontinuing any as-needed or routine orders
- When considering the risks, benefits, and burden of any prescription

Attempts to reduce or discontinue medications should be done selectively, one medication at a time. Medications may have been initially prescribed many years previously for a chronic condition, and newer agents with improved side effect profiles may be available. In some patients, addiction and dependence issues may arise. Regular comprehensive assessments of the patient are crucial, with the appropriate and necessary referrals made to psychiatry, psychology, addiction specialists, pain management, and other specialists as necessary. Certain medications should not be abruptly stopped and should instead be slowly reduced with medical supervision. This includes benzodiazepines and opioids (due to risk of symptoms of drug withdrawal). As noted, co-prescribing opioids and CNS depressants (e.g., benzodiazepines) should be avoided, if possible. Co-administration increases the risk of opioid toxicity, CNS depression, and death.

CONSIDERATIONS FOR SPECIAL POPULATIONS

Older Adults

By 2025, the number of adults 65 years of age and older in the United States is projected to increase 80% from 2010 estimates, comprising nearly 20% of the population. Understanding age-related physiologic changes and the complexity of pain management in elderly patients is essential for optimal efficacy, safety, and tolerability [81].

Independent of disease morbidity, aging elevates the risk of adverse events and associated opioid toxicity. The elderly account for 49% of all hospitalizations due to medication adverse effects [82]. A variety of age-related physiologic changes account for this, including diminished gastric secretions and intestinal dysmotility; vitamin D deficiency, loss of appetite, and poor nutrition; and decreased bone density. Increased arterial thickening and rigidity elevate cardiac risk, while decreased lung elasticity may exacerbate respiratory disorders. Neurons become less stress-resilient. Reduced hepatic and renal blood flow diminish metabolism and filtration, increasing the risk for toxic substance accumulation [82]. Patients with dementia and/or cognitive deficits may have communication problems or confusion that render expression of pain severity, therapeutic response, and/or side effects difficult [83].

In older adults, heightened sensitivity to adverse effects results from physiologic changes, drug interactions, and drug-disease interactions [84]. Aging is associated with higher steady-state concentrations of water-soluble drugs and increased half-life of fat-soluble drugs. Consequently, opioid use in older adults may necessitate a lower than usual dose or longer dosage interval in order to maintain an appropriate balance between analgesia and side effect risk [85]. Other functional changes and comorbidities that impact opioid pharmacokinetics may also influence patient response and tolerability. Therefore, the selection and prescribed dosage of opioids in elderly patients must be considered carefully [83].

Older adults are also more likely to be prescribed multiple medications for a variety of chronic and acute conditions. In some cases of multimorbidity and chronic conditions (e.g., hypertension), the use of multiple medications may be unavoidable if one is to follow best practice clinical guidelines; this is referred to as "appropriate polypharmacy." However, even when the prescription of multiple medications is warranted, it raises the risks of drug-drug interactions, compliance issues, and adverse effects.

Elderly adults are more likely than younger adults to experience significant chronic pain because of the higher prevalence of rheumatic diseases, orthopedic conditions, and other debilitating illnesses. In many cases, opioid therapy with optimum patient-treatment matching is the safest analgesic option for elderly patients compared with oral NSAIDs, acetaminophen, antidepressants, or anticonvulsants [81].

Woman Who Are or May Become Pregnant

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, preterm delivery, and birth defects [18]. 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. 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 [18].

Patients with Mental Health Conditions

Because psychologic 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, might help clinicians improve overall pain treatment outcomes [18]. Experts noted that clinicians should use additional caution and increased monitoring 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. 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. 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 [18].

Non-English-Proficient Patients

For patients who are not proficient in English, it is important that information regarding the risks associated with the use of opioids and available resources be provided in their native language, if possible. When there is an obvious disconnect in the communication process between the practitioner and patient due to the patient's lack of proficiency in the English language, an interpreter is required. Interpreters can be a valuable resource to help bridge the communication and cultural gap between patients and practitioners. Interpreters are more than passive agents who translate and transmit information back and forth from party to party. When they are enlisted and treated as part of the interdisciplinary clinical team, they serve as cultural brokers who ultimately enhance the clinical encounter. In any case in which information regarding treatment options and medication/treatment measures are being provided, the use of an interpreter should be considered. Print materials are also available in many languages, and these should be offered whenever necessary.

IDENTIFICATION OF DRUG DIVERSION/SEEKING BEHAVIORS

Research has more closely defined the location of prescribed opioid diversion into illicit use in the supply chain from the manufacturer to the distributor, retailer, and the end user (the pain patient). This information carries with it substantial public policy and regulatory implications. The 2020 National Survey on Drug Use and Health asked 9.3 million non-medical users of prescription opioids how they obtained their most recently used drugs [86]. Among persons 12 years of age or older, 47.2% obtained their prescription opioids from a friend or relative. Of this, 34.4% got them through a friend or relative for free, 9.2% bought them from a friend or relative, and 3.7% took them from a friend or relative without asking [86]. Another 42.0% got their opioids through a prescription from one doctor (vs. 35.4% in 2016) [86]. Less frequent sources included a drug dealer or other stranger (6.2%); multiple doctors (1.0%); and theft from a doctor's office, clinic, hospital, or pharmacy (0.6%) (vs. 0.7% in 2016) [86]. In total, 9.3 million people diverted and misused pain relievers (including prescription opioids) in the past year, 6.2 million misused tranquilizers or sedatives and 1.8 million misused stimulants [86].

The most common drugs diverted from healthcare facilities are opioids, and drugs stolen from healthcare facilities are typically used to support an addiction of the healthcare worker or an associate or, less commonly, for sale for financial gain [87]. This theft can be of unopened vials; vials or syringes that have been tampered with, resulting in either substituted or diluted dosages being administered to the patient; or residual drug left in a syringe or vial after only a fraction of the drug that has been signed out was actually administered to the patient. In addition, this theft can be of discarded syringes or ampules that have been properly disposed of in a "sharps" safety container [87].

In the healthcare setting, the following factors are considered contributors to controlled substance diversion [88]:

- Excess ordering
- Unsupervised access to drug storage areas
- Unverified verbal orders
- Flexible ordering and administration
- Forgery and/or falsification of patient documentation
- Compounding and repackaging
- Typical doses smaller than stocked drugs
- Poor verification of dispensing to clinical units
- Reduced pharmacy oversight of dispensing with introduction of technology (e.g., automated dispensing cabinets)
- Loopholes in the intended use of or poorly configured automated dispensing cabinets
- Prepared drugs are unsupervised and unsecured
- Unsupervised access to drug stock in patient care areas
- Visual confirmation of or falsification of witnessing wasting
- Falsification of drug expiration
- Presence of partially administered drugs on clinical units
- Unsecured waste receptacles

Many of these same factors contribute to the theft of controlled substances from healthcare facilities by patients, visitors, vendors, and various other opportunists.

As discussed, UDTs can give insight into patients who are misusing opioids. A random sample of UDT results from 800 pain patients treated at a Veterans Affairs facility found that 25.2% were negative for the prescribed opioid while 19.5% were positive for an illicit drug/unreported opioid [89]. Negative UDT results for the prescribed opioid do not

necessarily indicate diversion but may indicate the patient halted his/her use due to side effects, lack of efficacy, or pain remission. The concern arises over the increasingly stringent climate surrounding clinical decision-making regarding aberrant UDT results and that a negative result for the prescribed opioid or a positive UDT may serve as the pretense to terminate a patient rather than guide him/her into addiction treatment or an alternative pain management program [90].

In addition to aberrant urine screens, there are certain behaviors that are suggestive of an emerging opioid use disorder. The most suggestive behaviors are [70; 91; 92]:

- Selling medications
- Prescription forgery or alteration
- Injecting medications meant for oral use
- Obtaining medications from nonmedical sources
- Resisting medication change despite worsening function or significant negative effects
- Loss of control over alcohol use
- Using illegal drugs or non-prescribed controlled substances
- Recurrent episodes of:
  - Prescription loss or theft
  - Obtaining opioids from other providers in violation of a treatment agreement
  - Unsanctioned dose escalation
  - Running out of medication and requesting early refills

Behaviors with a lower level of evidence for their association with opioid misuse include [70; 91; 92]:

- Aggressive demands for more drug
- Asking for specific medications
- Stockpiling medications during times when pain is less severe
- Using pain medications to treat other symptoms
- Reluctance to decrease opioid dosing once stable
- In the earlier stages of treatment:
  - Increasing medication dosing without provider permission
  - Obtaining prescriptions from sources other than the pain provider
  - Sharing or borrowing similar medications from friends/family

INTERVENTIONS FOR SUSPECTED OR KNOWN ADDICTION OR DRUG DIVERSION

Very simply, drug diversion is defined as the unlawful deflection of prescription drugs from medical sources into the illegal market; this includes sharing drugs with persons who does not have a valid prescription, even if no money or other materials are exchanged. Drug diversion contributes to overdose morbidity and mortality, crime, increased healthcare costs, disease outbreaks, and violence in society and in healthcare facilities. There are a number of actions that prescribers and dispensers can take to prevent or intervene in cases of drug diversion. These actions can be generally categorized based on the various mechanisms of drug diversion.

Prevention is the best approach to addressing drug diversion. As noted, the most common source of nonmedical use of prescribed opioids is from a family member or friend, through sharing, buying, or stealing. To avoid drug sharing among patients, healthcare professionals should educate patients on the dangers of sharing opioids and stress that "doing prescription drugs" is the same as "using street drugs" [75]. In addition, patients should be aware of the many options available to treat chronic pain aside from opioids. To prevent theft, patients should be advised to keep medications in a private place and to refrain from telling others about the medications being used.

Communication among providers and pharmacies can help to avoid inappropriate attainment of prescription drugs through "doctor shopping." Prescribers should keep complete and up-to-date records for all controlled substance prescribing. When possible, electronic medical records should be integrated between pharmacies, hospitals, and managed care organizations [75]. If available, it is also best practice to periodically request a report from the state's prescription reporting program to evaluate the prescribing of opioids to your patients by other providers [75].

When dealing with patients suspected of drug seeking/diversion, first inquire about prescription, over-the-counter, and illicit drug use and perform a thorough examination [75; 93]. Pill counting and/or UDT may be necessary to investigate possible drug misuse. Photo identification or other form of identification and social security number may be required prior to dispensing the drug, with proof of identity documented fully. If a patient is displaying suspicious behaviors, consider prescribing for limited quantities [93].

If a patient is found to be abusing prescribed opioids, this is considered a violation of the treatment agreement and the clinician must make the decision whether or not to continue the therapeutic relationship. If the relationship is terminated, it must be done ethically and legally. The most significant issue is the risk of patient abandonment, which is defined as ending a relationship with a patient without consideration of continuity of care and without providing notice to the patient. The American Medical Association Code of Ethics states that physicians have an obligation to support continuity of care for their patients. While physicians have the option of withdrawing from a case, they should notify the patient (or authorized decision maker) long enough in advance to permit the patient to secure another physician and facilitate transfer of care when appropriate [94]. Patients may also be given resources and/or recommendations to help them locate a new clinician.

Patients with chronic pain found to have an ongoing substance abuse problem or addiction should be referred to a pain specialist for continued treatment. If drug diversion has occurred, the activity should be documented and a report to law enforcement should be made [95]. The DEA requires that registrants notify the Field Division Office of the Administration in his/her area, in writing, of the theft or significant loss of any controlled substances within one business day of discovery of such loss or theft. This is followed by completion of DEA Form 106 and submission of that report to the DEA and the Board. With respect to the initial notification to the DEA, the New Orleans Field Division has established an email address to facilitate that report. Please direct your initial report of theft/loss of controlled substances to NOFD.theftorloss@DEA.gov. DEA 106 reports may also be submitted to the DEA electronically at https://www.deadiversion.usdoj.gov/21cfr_reports/theft/index.html.

The Louisiana Administrative Code requires that any theft or unexplained loss of controlled substances in the possession of a registrant shall be reported by the registrant to the board, in writing, within 10 days of the date of the registrant's discovery of such theft or loss, but in no event later than 10 days following the completion of the quarterly physical inventory next following such theft or loss [96]. Such written report shall state the date or estimated date of such theft or loss, the generic chemical or trade name, amount or quantity, and dosage form and strength of any medications stolen or lost, and a detailed description of the circumstances surrounding the theft or loss.

COMPLIANCE WITH STATE AND FEDERAL LAWS

In response to the rising incidence in prescription opioid abuse, addiction, diversion, and overdose since the late 1990s, the FDA has mandated opioid-specific REMS to reduce the potential negative patient and societal effects of prescribed opioids. Other elements of opioid risk mitigation include FDA partnering with other governmental agencies, state professional licensing boards, and societies of healthcare professionals to help improve prescriber knowledge of appropriate and safe opioid prescribing and safe home storage and disposal of unused medication [66].

Several regulations and programs at the state level have been enacted in an effort to reduce prescription opioid abuse, diversion, and overdose, including [97]:

- Physical examination required prior to prescribing
- Tamper-resistant prescription forms
- Pain clinic regulatory oversight
- Prescription limits
- Prohibition from obtaining controlled substance prescriptions from multiple providers
- Patient identification required before dispensing
- Immunity from prosecution or mitigation at sentencing for individuals seeking assistance during an overdose

CONTROLLED SUBSTANCES LAWS/RULES

The U.S. Drug Enforcement Administration (DEA) is responsible for formulating federal standards for the handling of controlled substances. In 2011, the DEA began requiring every state to implement electronic databases that track prescribing habits, referred to as PDMPs. Specific policies regarding controlled substances are administered at the state level [98].

According to the DEA, drugs, substances, and certain chemicals used to make drugs are classified into five distinct categories or schedules depending upon the drug's acceptable medical use and the drug's abuse or dependency potential [99]. The abuse rate is a determinate factor in the scheduling of the drug.

Schedule I controlled substances have no currently accepted medical use in the United States, a lack of accepted safety for use under medical supervision, and a high potential for abuse. Some examples of substances listed in Schedule I are: heroin, lysergic acid diethylamide (LSD), marijuana (cannabis), peyote, methaqualone, and 3,4-methylenedioxymethamphetamine ("Ecstasy") [100].

Schedule II/IIN substances have an accepted medical use but also a high potential for abuse, which may lead to severe psychologic or physical dependence. Examples of Schedule II/IIN narcotics include amphetamine, hydromorphone, methadone, meperidine, methylphenidate, oxycodone, fentanyl, morphine, opium, codeine, pentobarbital, and hydrocodone [100].

Schedule III/IIIN controlled substances have a potential for abuse less than substances in Schedules I or II and abuse may lead to moderate or low physical dependence or high psychologic dependence. Examples of Schedule III/IIIN narcotics include products containing not more than 90 mg of codeine per dosage unit (e.g., Tylenol with Codeine), buprenorphine, benzphetamine, phendimetrazine, ketamine, and anabolic steroids [100].

Schedule IV controlled substances have a low potential for abuse relative to substances in Schedule III. Examples include alprazolam, carisoprodol, clonazepam, diazepam, lorazepam, midazolam, temazepam, and triazolam [100].

Schedule V controlled substances have a low potential for abuse relative to substances listed in Schedule IV and consist primarily of preparations containing limited quantities of certain narcotics. Examples of Schedule V substances include ezogabine and cough preparations containing not more than 200 mg of codeine per 100 mL or 100 g [100].

LOUISIANA LAWS AND RULES

Most states have established laws and rules governing the prescribing and dispensing of opioid analgesics. It is each prescriber's responsibility to have knowledge of and adhere to the laws and rules of the state in which he or she prescribes.

Act 76 of the 2017 Regular Session of the Louisiana Legislature

In 2017, the Louisiana Legislature passed Act 76, which includes requirements for prescribers in the state. As of that year, prescribing practitioners applying for an initial controlled dangerous substance license or renewing of such a license from the Louisiana Board of Pharmacy will be automatically registered as a participant in the PDMP. A prescriber or his/her delegate must access and review a patient's record in the PDMP prior to prescribing any opioid for the patient, and must access and review the record in the PDMP at least every 90 days if the patient's course of treatment continues for more than 90 days. This requirement does not apply if [101]:

- The drug is prescribed to a hospice or any other patient diagnosed as terminally ill.
- The drug is prescribed or administered for the treatment of cancer-related chronic or intractable pain.
- The drug is ordered or administered to a patient being treated in a hospital.
- The PDMP is not accessible or not functioning due to an electronic issue. However, the prescriber must check the PDMP after electronic accessibility has been restored, and note the cause for the delay in the patient's chart.
- No more than a single seven-day supply of the drug is prescribed or administered to a patient.

Act 76 also established a mandate for all professionals with a controlled dangerous substance license to complete a one-time continuing education requirement for three hours of continuing education pertaining to drug diversion training, best practices regarding prescribing of controlled substances, and appropriate treatment for addiction [101].

Act 82 of the 2017 Regular Session of the Louisiana Legislature

Also in 2017, the Legislature passed Act 82, which sets limits on new opioid prescriptions, with the ultimate goal of appropriately treating pain while also preventing diversion [102]. With the exception of medications used for the treatment of substance abuse or dependence, when issuing a first-time opioid prescription for outpatient use to an adult patient with an acute condition, a medical practitioner shall not issue a prescription for more than a seven-day supply. In addition, a medical practitioner shall not issue a prescription for an opioid to a minor for more than a seven-day supply at any time and shall discuss with a parent, tutor, or guardian of the minor the risks associated with opioid use and the reasons why the prescription is necessary.

There is a general exception to these limits. If, in the professional medical judgment of a medical practitioner, more than a seven-day supply of an opioid is required to treat the adult or minor patient's acute medical condition or is necessary for the treatment of chronic pain management, pain associated with a cancer diagnosis, or for palliative care, the practitioner may issue a prescription for the quantity needed to treat the patient's acute medical condition or pain. The condition triggering the prescription of an opioid for more than a seven-day supply should be clearly documented in the patient's medical record and the practitioner shall indicate that a nonopioid alternative was not appropriate to address the medical condition [102].

Act 82 also requires that prior to issuing a prescription for an opioid, a medical practitioner must [102]:

- Consult with the patient regarding the quantity of the opioid and the patient's option to fill the prescription in a lesser quantity.
- Inform the patient of the risks associated with the opioid prescribed.

A pharmacist filling a prescription for an opioid may dispense the prescribed substance in an amount less than the recommended full quantity indicated on the prescription if requested by the patient and the prescription complies with the law. The patient may request that the pharmacist fill an additional amount not to exceed the remaining prescribed quantity. If the dispensed amount is less than the recommended full quantity, the pharmacist or a designee shall ensure that the actual dispensed amount is accurately recorded in the prescription monitoring program. The pharmacist or a designee shall also, within seven days, make a notation in the interoperable electronic health record of the patient, if the pharmacist has access to the record.

The Louisiana Prescription Monitoring Program

Emerging trends and patterns of prescription opioid abuse, addiction, and overdose are monitored by several industry and government agencies through data collection from a variety of sources. These include health insurance claims; the Automation of Reports and Consolidated Orders System, a DEA-run program that monitors the flow of controlled substances from manufacturing through distribution to retail sale or dispensing; the Treatment Episode Data Set, which monitors treatment admissions; the National Center for Health Statistics state mortality data; and the Researched Abuse, Diversion, and Addiction-Related Surveillance System, which monitors prescription drug abuse, misuse, and diversion [103; 104; 105; 106; 107].

Almost all states, including Louisiana, have enacted PDMPs to facilitate the collection, analysis, and reporting of information on controlled substances prescribing and dispensing. The Louisiana Prescription Monitoring Program is a statewide comprehensive platform for healthcare professionals to review patients' controlled substance prescription history more quickly and efficiently. The goal is to minimize any workflow disruption by providing near-instant and seamless access to critical controlled substance prescription history information to both prescribers and pharmacists. This platform utilizes current PDMP prescription data and transfers it into electronic health records and pharmacy management systems. This statewide integration is a key component of Louisiana's ongoing efforts to address the opioid crisis. Accessing and viewing a patient's PMP report obtained through the integration platform complies with Louisiana's PMP Mandatory Use Law (as modified by Acts 76 and 82) [108].

OPIOID MISUSE AND USE DISORDER

DEFINITIONS

A confusing aspect of the body of research on opioid abuse and dependence is the inconsistent use of important terminology that describes the nature and severity of involvement with therapeutic and illicit opioids. Misuse and misunderstanding of these concepts and their correct definitions has resulted in misinformation and represents an impediment to proper patient care. The following definitions have been proposed in an effort to encourage more correct usage of this terminology [1; 52; 109; 110; 111; 112]:

- **Misuse, nonmedical use**: Patients' use of an opioid that departs from intended prescribing, including use for an unintended purpose, exceeding the prescribed amount, or taking the drug more frequently or for longer than prescribed.
- **Abuse**: Definition varies widely depending on the context, but generally means a maladaptive pattern of use with the primary intent of achieving euphoria or getting high. The Drug Enforcement Administration (DEA) defines abuse as the use of a schedule II through V drug in a manner or amount inconsistent with the medical or social pattern of a culture. The American Psychiatric Association defines abuse as "a maladaptive pattern of substance use, leading to clinically significant impairment or distress as manifested by one or more behaviorally based criteria."
- **Addiction**: Defined by the American Society of Addiction Medicine (ASAM) as "a treatable, chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual's life experiences." It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving.
- **Dependence**: This term has replaced the term "addiction" in some contexts. Opioid dependence refers to both psychologic dependence (or addiction) and physical dependence. Physical dependence consists of neurobiologic adaptation (development of tolerance) from chronic exposure.
- **Recovery**: In the context of substance use disorders, this term refers to the process and tools used by a person wishing to stop using drugs and resume a productive life.

The fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) defines opioid use disorder as a problematic pattern of opioid use, leading to clinically significant impairment or distress. Opioid use disorder may be diagnosed if a patient exhibits two or more of the following [7; 110]:

- Opioids taken in larger amounts or over a longer period than was intended
- A persistent desire or unsuccessful efforts to cut down or control use
- A great deal of time is spent in activities necessary to obtain, use, or recover from use
- Craving, or a strong desire or urge to use
- Recurrent opioid use resulting in failure to fulfill major role obligations at work, school, or home
- Continued use despite having persistent or recurrent social or interpersonal problems caused by or exacerbated by use
- Important social, occupational, or recreational activities are given up or reduced because of use
- Recurrent use in situations in which it is physically hazardous
- Continued use despite knowledge of having a persistent or recurrent physical or psychologic problem that is likely to have been caused by or exacerbated by use
- Tolerance
- A need for markedly increased amounts to achieve intoxication or desired effect

- A markedly diminished effect with continued use of the same amount
- Withdrawal

Note: The criteria for tolerance and withdrawal are not considered to be met for those taking opioids solely under appropriate medical supervision.

In summary, the term dependence is used to describe two separate phenomena. Pharmacologically, drug dependence is characterized by the presence of tolerance and a withdrawal syndrome. Psychiatrically, drug dependence is characterized by compulsive use, inability to reduce use, preoccupation, drug-seeking behaviors, and a heightened vulnerability to relapse after abstinence [113].

NATURAL HISTORY AND PATHOPHYSIOLOGY

Although the time from initiation to daily use and serious physiologic and psychologic dependence is highly variable, the different stages of opioid dependence are clearly delineated [113]. These stages include initiation, continuation, withdrawal, and relapse. Each stage is characterized by specific neurotransmitter action, involvement of specific brain structures, and activation of specific neural circuits. An understanding of these different processes is crucial to develop an understanding of the therapeutic strategies [114].

Opioid dependence is best described as a central nervous system disorder characterized by neurobiologic changes leading to compulsive drug-taking behaviors. As the result of chronic use, the cells producing endogenous opioids cease to function and degenerate, causing the user to become physically dependent on exogenous opioids [115].

According to the classical theory of addiction, opioid dependence results from the need to reduce distress, as withdrawal is a physical expression of distress. This is referred to as negatively reinforced behavior. This hypothesis has been challenged by the finding that the degree of physical dependence does not predict the intensity of subsequent craving, nor does detoxification and recovery from physical dependence prevent recidivism. Additionally, the motivational aspects of withdrawal are independent of the intensity and pattern of the physical symptoms of withdrawal [116].

Alternative hypotheses focus on the role of the mesocorticolimbic dopamine system, an anatomical pathway that originates from the ventral tegmental area in the midbrain and projects to several forebrain regions, including the nucleus accumbens and medial prefrontal cortex [116]. Dependence on most drugs of abuse is characterized by an altered physiologic state inferred from the emergence of a withdrawal syndrome following cessation of drug administration. Alleviation of an increasingly severe, withdrawal-induced negative affective state may reinforce continued drug taking and directly contribute to the development of dependence [117].

SCREENING

Regular screenings in primary care and other healthcare settings enables earlier identification of mental health and substance use disorders, which translates into earlier care. Screenings should be provided to people of all ages, even the young and the elderly. The National Institute on Drug Abuse has identified the following evidence-based screening tools and assessment resource materials as potentially useful for this process [118]:

- Screening to Brief Intervention (S2BI)
- Brief Screener for Alcohol, Tobacco, and other Drugs (BSTAD)
- Tobacco, Alcohol, Prescription medication, and other Substance use (TAPS)
- Opioid Risk Tool
- CRAFFT
- Drug Abuse Screen Test (DAST-10 or DAST-20: Adolescent version)
- Screening, Brief Intervention, and Referral to Treatment (SBIRT)

Tobacco, Alcohol, Prescription medication, and other Substance use (TAPS)

The TAPS Tool consists of a combined screening component followed by a brief assessment for those who screen positive [119]. If a patient responds positively (i.e., any response other than "never") to ever using tobacco, alcohol, illicit drugs, and/or non-medical use of prescription drugs, a series of brief substance-specific assessment questions are asked to arrive at a risk level for that substance.

Screening, Brief Intervention, and Referral to Treatment (SBIRT)

SBIRT is an evidence-based practice used to identify, reduce, and prevent problematic use, abuse, and dependence on alcohol and illicit drugs. It is an early intervention approach that targets those with nondependent substance use to provide effective strategies for intervention prior to the need for more extensive or specialized treatment [120; 121].

The first component of the SBIRT process is screening, which provides a quick and simple method of identifying patients who use substances at at-risk levels, as well as those who are already experiencing substance use-related issues. The typical screening process involves the use of a brief one-to-three question prescreen. If a person screens positive on one of these screening instruments, they would then be given a longer alcohol or drug use screening. The screens usually assess patient self-reported information about substance use, and any healthcare professional can easily score the results [121].

The next step is brief intervention. In primary care settings, brief interventions last from 5 minutes of brief advice to 15 to 30 minutes of brief counseling. Brief interventions are not intended to treat people with serious substance dependence, but rather to treat problematic or risky substance use. Skillfully conducted, brief interventions are essential to successful SBIRT implementation. The two most common behavioral therapies used in SBIRT programs are brief versions of cognitive behavioral therapy and motivational interviewing, or some combination of the two [121].

Referral to treatment is a critical yet often overlooked component of the SBIRT process. It involves establishing a clear method of follow-up with patients that have been that have been identified as having a possible dependency on a substance or in need of specialized treatment [121]. The referral to treatment process consists of assisting a patient with accessing specialized treatment, selecting treatment facilities, and helping navigate any barriers such as treatment cost or lack of transportation that could hinder treatment in a specialty setting [120].

TREATMENT

Management of opioid dependence entails different methods to achieve different goals, depending on the health situation and treatment history of the patient. These treatment approaches include [114]:

- Crisis intervention: Directed at immediate survival by reversing the potentially lethal effects of overdose with an opioid antagonist.
- Harm reduction: Intended to reduce morbidity and mortality associated with use of dirty needles and overdose.
- Detoxification/withdrawal: Aims to remove the opioid of abuse from the patient's body, either through gradual taper and substitution of a long-acting opioid or through ultra-rapid opioid detoxification.
- Maintenance treatment or opioid (agonist) replacement therapy: Also known as medication-assisted treatment, this therapy is aimed at reduction/elimination of illicit opioid use and lifestyle stabilization. Maintenance follows detoxification/withdrawal, whereby the patient is tapered from short-acting opioids and introduced to a long-acting opioid agonist, such as methadone or buprenorphine. Patients remain on agonist therapy short-term, long-term, or indefinitely depending on individual needs.

- Abstinence-oriented therapy: Treatment directed at cure. The patient is tapered off of short-acting opioids during the detoxification/withdrawal process and may be placed on an opioid antagonist with the goal of minimizing relapse.

All treatment approaches share the common goal of improving health outcomes and reducing drug-related criminality and public nuisance [114].

Crisis Intervention: Management of Overdose

Individuals who have first contact with persons suspected of experiencing an opioid-related overdose are in the position to intervene to prevent the potentially devastating consequences. In these cases, care begins with crisis intervention directed at immediate survival by reversing the potentially lethal effects of overdose with an opioid antagonist.

Opioid antagonists have obvious therapeutic value in the treatment of opioid overdose. A 2015 study found that wider distribution of naloxone and training in its administration might have prevented numerous deaths from opioid overdoses in the United States [122]. Since the first community-based opioid overdose prevention program began distributing naloxone in 1996, more than 26,000 overdoses have been reversed [122].

In Louisiana, a licensed medical practitioner may, directly or by standing order, prescribe or dispense opioid antagonists without having examined the individual to whom it may be administered if [123]:

- The individual receiving and administering the naloxone or other antagonist is given all training required by the Department of health for the safe and proper administration of the drug to persons who are or are believed to be overdosing on an opioid-related drug.
- The antagonist is prescribed or dispensed in a manner that it is administered through an FDA-approved device.

The Department of Health has implemented a standing order for naloxone, allowing participating pharmacists to dispense naloxone (including refills) to state residents without a formal prescription. Naloxone is generally covered by the state Medicaid program, and there is a Good Samaritan Law [12]. The U.S. Department of Health and Human Services has recommended that naloxone be prescribed or provided to patients prescribed opioids who [124]:

- Are receiving opioids at a dosage of 50 morphine mg equivalents (MME) per day or greater
- Have respiratory conditions such as chronic obstructive pulmonary disease (COPD) or obstructive sleep apnea (regardless of opioid dose)
- Have been prescribed benzodiazepines (regardless of opioid dose)
- Have a non-opioid substance use disorder, report excessive alcohol use, or have a mental health disorder (regardless of opioid dose)
- Are at high risk for experiencing or responding to an opioid overdose, including individuals:
- Using heroin, illicit synthetic opioids or misusing prescription opioids
- Using other illicit drugs such as stimulants, including methamphetamine and cocaine, which could potentially be contaminated with illicit synthetic opioids like fentanyl
- Receiving treatment for opioid use disorder, including medication-assisted treatment with methadone, buprenorphine, or naltrexone
- With a history of opioid misuse that were recently released from incarceration or other controlled settings where tolerance to opioids has been lost

Opioid Antagonists

Relatively minor changes in the structure of an opioid can convert an agonist drug into one with antagonistic actions at one or more opioid receptor types. Opioid antagonists include naloxone, naltrexone, and nalmefene. Interestingly, naloxone also appears to block the analgesic effects of placebo medications and acupuncture. These agents have little or no potential for abuse [125].

In response to acute overdose, the short-acting opioid antagonist naloxone is considered the criterion standard, and it remains the most widely used opioid antagonist for the reversal of overdose and opioid-related respiratory depression. It acts by competing with opioids at receptor sites in the brain stem, reversing desensitization to carbon dioxide, and reversing or preventing respiratory failure and coma. There is no evidence that subcutaneous or intramuscular use is inferior to intravenous naloxone. This has prompted some states, including West Virginia, to pass laws allowing opioid antagonists to be available to the general public for administration outside the healthcare setting to treat acute opioid overdose [114].

When used for opioid overdose, a dose of 0.4–2 mg of naloxone is administered intravenously, intramuscularly, or subcutaneously [126]. If necessary, the dose may be repeated every 2 to 3 minutes for full reversal. For ease of use, naloxone is also available in a pre-filled auto-injection device. An intranasal formulation is also available in doses of 2 mg, 4 mg, or 8 mg [126]. It is important that standard Advanced Cardiac Life Support (ACLS) protocols be continued while naloxone is being administered and that medical treatment (at a healthcare facility) be given immediately.

Harm Reduction

Harm reduction measures are primarily employed to minimize the morbidity and mortality from opioid abuse and to reduce public nuisance [127]. As a part of this effort, measures to prevent and minimize the frequency and severity of overdoses have been identified. Enrollment in opioid substitution therapy, with agents such as methadone and buprenorphine, substantially reduces the risk of overdose as well as the risk for infection and other sequelae of illicit opioid use [127].

Detoxification and Withdrawal

The process of tapering opioid-dependent patients from agonist therapy is often referred to as detoxification, or more accurately, medically supervised withdrawal [128; 129]. Its purpose is to eliminate physical dependence on opioid medications. It can be considered the medically supported transition to a medication-free state or to antagonist therapy. A careful and thorough review of the risks and benefits of detoxification should be provided and informed consent obtained from patients prior to choosing this option [129; 130]. Detoxification alone should not be considered a treatment and should only be promoted in the context of a well-planned relapse-prevention program [114; 129].

Discontinuation of opioid use must be implemented slowly and cautiously to avoid a marked abstinence syndrome. Withdrawal symptoms may not begin for days after abrupt discontinuation of methadone or buprenorphine given their longer half-lives. Protracted abstinence, or post-acute withdrawal, may last for several months and is characterized by asthenia, depression, and hypotension. Post-acute withdrawal is more likely to occur with methadone than other opioids [128].

The three primary treatment modalities used for detoxification are opioid agonists, non-opioid medications, and rapid and ultra-rapid opioid detoxification [128]. The most frequently employed method of opioid withdrawal is a slow, supervised detoxification during which an opioid agonist, usually methadone, is substituted for the abused opioid [115]. Methadone is the most frequently used opioid agonist due to the convenience of its once-a-day dosing [128]. Methadone is highly bound to plasma proteins and accumulates more readily than heroin in all body tissues. Methadone also has a longer half-life, approximately 22 hours, which makes withdrawal more difficult than from

heroin. Substitution therapy with methadone has a high initial dropout rate (30% to 90%) and an early relapse rate. Alternative pharmacologic detoxification choices (all off-label) include clonidine (with or without methadone), midazolam, trazodone, or buprenorphine [115; 131; 132; 133].

Many opioid withdrawal symptoms, such as restlessness, rhinorrhea, lacrimation, diaphoresis, myosis, piloerection, and cardiovascular changes, are mediated through increased sympathetic activation, the result of increased neuron activity in the locus coeruleus. Non-opioid agents (such as clonidine), which inhibit hyperactivation of noradrenergic pathways stemming from the locus coeruleus nucleus, have been used to manage acute withdrawal [115; 131]. The first non-opioid treatment approved for the management of opioid withdrawal symptoms is lofexidine [134]. In studies, lofexidine resulted in less severe withdrawal symptoms and greater treatment retention than placebo.

However, some withdrawal symptoms, including anxiety and myalgias, are resistant to clonidine; benzodiazepines and nonsteroidal anti-inflammatory agents may be necessary to treat these symptoms. To mitigate withdrawal symptoms and assist in detoxification, alpha2-agonists, opioid agonist-antagonists, benzodiazepines, and antidepressants have been used [115; 131.

Following detoxification, patients may feel exhausted and weak. Other complications, such as slight variations in hemodynamic status and gastrointestinal tract symptoms, follow quickly and may take several days to resolve. Muscle cramps and low back pain can be treated with nonsteroidal anti-inflammatory drugs [131]. However, the newer cyclooxygenase-2 (COX-2) inhibitors may be advantageous because they produce fewer gastrointestinal side effects [115]. Insomnia is a frequent aspect of acute and protracted withdrawal, as opioids disrupt the normal sleep-wake cycle and many addicts require narcotics to sleep. Although long-term disruption of the normal sleep-wake cycle cannot be corrected rapidly, melatonin (3 mg), benzodiazepines, or antihistamines can be used with beneficial effects. Hypnosis and relaxation techniques are nonpharmacologic methods that may also be used [115]. Psychosocial treatments offered in addition to pharmacologic detoxification treatments may positively impact treatment retention and completion, results at follow-up, and compliance [135; 136].

Agonist Replacement or Abstinence Therapy

Two principle treatment modalities are offered for opioid-dependent patients: agonist maintenance (also referred to as medication-assisted treatment) or detoxification followed by outpatient or residential drug-free treatment. Both can be effective, with no clear indication for each, although agonist maintenance leads to greater treatment retention [137]. A reasonable approach is initial outpatient or residential treatment referral for patients relatively new to treatment, with agonist maintenance appropriate for patients with history of treatment failures, greater disease severity, or a history of drug overdoses. Naltrexone is best reserved for patients with strong legal incentives to abstain, family involvement to monitor treatment, or concurrent enrollment and involvement in a psychosocial intervention [138].

At present, there are no direct interventions that are capable of reversing the effects of drugs of dependence on learning and motivation systems [139]. Instead, the management of opioid dependence often consists of pharmacotherapy with methadone and buprenorphine, which do not eliminate physical dependence on opioids. These medications instead reduce the use of illicit opioids and produce very strong positive health outcomes as measured by decreased mortality, improved mental and physical health, and reduced risk of disease transmission [139]. Considering the high rate of relapse after detoxification, medication-assisted treatment with methadone or buprenorphine is currently considered to be the first-line treatment for opioid-dependent patients [114]. However, outpatient medication-assisted treatment is not a viable option for patients who are pregnant, with comorbid benzodiazepine or alcohol dependence (risk of overdose), with severe unstable psychiatric conditions, and/or with acute or severe liver disease [140].

Effective use of medication-assisted treatment in the outpatient setting requires access to the agonist and a support system to reinforce accountability. Prior to initiating agonist maintenance therapy, the patient and all members of the interprofessional care team should be aware of the treatment goals, expectations and responsibilities, and potential risks [140]. The Substance Abuse and Mental Health Services Administration has identified best practices when prescribing medication for the treatment of opioid use disorder [141]:

- Assess the need for treatment
- Educate the patient about how the medication works and the associated risks and benefits; obtain informed consent; and educate on overdose prevention
- Evaluate the need for medically managed withdrawal from opioid
- Address co-occurring disorders
- Integrate pharmacologic and non-pharmacologic therapies
- Refer patients for higher levels of care, if necessary

Any treatment for opioid dependence must take into consideration the chronic relapsing nature of opioid dependence, characterized by a variable course of relapse and remission in many patients. Treatments should emphasize patient motivation, psychoeducation, continuity of care, integration of pharmacotherapy and psychosocial support, and improved liaison between the treatment staff and the judicial system. Pharmacotherapy should be offered in a comprehensive healthcare context that also addresses the psychosocial aspects of dependence [114; 141]. Due to the chronic nature of opioid use disorder, the need for continuing medication-assisted therapy should be re-evaluated periodically. There is no maximum recommended duration of maintenance treatment, and for some patients, treatment may continue indefinitely. Opioid-dependent patients frequently suffer from physical and psychiatric disorders, and targeted interventions of psychiatric comorbidity are essential in improving treatment outcome for these patients [114; 141]. Polysubstance abuse is the rule rather than the exception in opioid dependence, and concurrent use of other substances should be carefully monitored and treated when necessary [114; 141]. Incarceration should never automatically result in discontinuation of an existing treatment; imprisonment offers a window of opportunity to initiate or restart treatment with a necessary continuation after release [114; 141].

Agonist Replacement Therapy

The goal of opioid replacement therapy is to reduce illicit drug use and associated health risks, with secondary goals of reducing unsafe sexual practices, improving vocational and psychosocial functioning, and enhancing quality of life [128]. The theoretical basis of opioid replacement stems from the finding that chronic opioid use results in an endogenous opioid deficiency as a result of the down-regulation of opioid production. This creates overwhelming cravings and necessitates interventions that shift the dependent patient's attention and drive from obsessive preoccupation with the next use of opioids to more adaptive areas of focus, such as work, relationships, and non-drug leisure activities [128; 142].

The neurobiologic changes resulting from prolonged opioid exposure provide a rationale for specific pharmacotherapies, such as long-acting opioid agonists, that are aimed at stabilizing these complex systems [142; 143]. Opioid agonist maintenance treatment stabilizes brain neurochemistry by replacing short-acting opioids, which can create rapid changes in opioid levels in the serum and brain, with a long-acting opioid that has relative steady-state pharmacokinetics. Opioid agonist maintenance treatment is designed to have minimal euphoric effect, block the euphoria associated with administration of exogenous opioids (competitive antagonism), eliminate the risk of infectious disease and health consequences associated with injection drug use, and prevent opioid withdrawal [142; 143].

Successful maintenance treatment entails stabilization of opioid dependence through opioid receptor occupation. Positron emission tomography studies have revealed that only 25% to 35% of brain opioid receptors are occupied during steady-state methadone maintenance, suggesting that unoccupied opioid receptors disrupted during cycles of opioid abuse could normalize during methadone maintenance [128; 143]. Additionally, opioid replacement therapy blocks much of the euphoria from illicit heroin use. Long-term opioid agonist treatment also has a positive impact on public health, through significantly reducing overdose deaths, criminal activity, and the spread of infectious disease [128; 143].

As of 2020, 509,008 patients in the United States were enrolled in opioid replacement therapy in 1,754 opioid treatment programs [144]. However, this represents only an estimated 18% of all opioid-dependent patients. Although some have criticized the practice of methadone and buprenorphine therapy on the grounds that one opioid is merely being substituted for another, the clinical benefits strongly support this treatment modality [128]. When compared to active street heroin users, these benefits include a four-times lower HIV seroprevalence rates, 70% fewer crime-days per year, and a one-year mortality rate of 1% (versus 8%) [145].

Abstinence-Oriented Therapies

The primary goal of abstinence-oriented interventions is cure, which is defined as long-term, stable abstinence from all opioids. Abstinence is achieved in two phases: detoxification and relapse prevention. Outcomes in abstinence-oriented programs are generally poor [114; 146].

The primary goal of pharmacotherapy during detoxification is to alleviate opioid withdrawal severity and associated distress/medical complications and to enhance patient motivation to continue treatment. Withdrawal can also be reduced by psychosocial measures, such as contingency management or counseling, and as discussed, the addition of psychosocial therapy to pharmacologic treatment increases efficacy. Buprenorphine and clonidine are both used to manage withdrawal symptoms, but buprenorphine's advantages, compared with clonidine, are related to its favorable side effect profile and positive effects on well-being and psychosocial variables [114].

12-Step/Self-Help Programs

Twelve-step programs for opioid abuse and dependence include Narcotics Anonymous (NA) and Methadone Anonymous (MA) and are modeled after Alcoholics Anonymous (AA), an abstinence-based support and self-improvement program that is based on the 12-step model of recovery. AA has helped hundreds of thousands of alcoholics achieve sobriety [147]. The 12-step model emphasizes acceptance of dependence as a chronic, progressive disease that can be arrested through abstinence but not cured. Additional elements include spiritual growth, personal responsibility, and helping other addicted persons. By inducing a shift in the consciousness of the addict, 12-step programs offer a holistic solution and are a resource for emotional support [147]. Although research on efficacy and patient outcomes in NA and MA is very limited, many prominent researchers emphasize the important role that ongoing involvement in 12-step programs plays in recovery from substance abuse [148].

The understanding of drug dependence as a chronic and relapsing disorder has helped professionals gain a better comprehension of the vital role played by 12-step programs. Every patient attempting to recover from a substance use disorder will encounter a time when he or she faces urges to use without the resources or assistance of healthcare professionals. Twelve-step programs are not considered treatment, nor are they intended as substitutes for treatment. Instead, they are organizations that provide ongoing and indefinite support in the achievement and maintenance of abstinence and in personal growth and character development [148].

Part of the effectiveness of NA and MA is related to their ability to provide a competing and alternative reinforcer to drug use. Involvement in 12-step programs can enhance the quality of social support and the social network of the member, a potentially highly reinforcing aspect the person stands to forfeit if they resume drug using. Other reinforcing elements of 12-step involvement include recognition for increasingly durable periods of abstinence and frequent awareness of the consequences of drug and alcohol use through attendance of meetings [149]. Research shows that establishing a pattern of 12-step program attendance early in treatment predicts the level of ongoing involvement. Emphasis and facilitation of early engagement in a 12-step program involvement are key [150].

Acupuncture

Auricular acupuncture is the most common acupuncture approach for substance abuse, including opioid abuse and dependence, in the United States and the United Kingdom. This technique consists of bilateral insertion of acupuncture needles in the outer ears [151]. There is controversy surrounding the presumed mechanism of action of acupuncture. Western scientists attempt to explain its action on the body's electromagnetic system, with the acupuncture needle creating a difference in electrical potential that stimulates extracellular ion flow. Chinese practitioners, who have been using acupuncture for several thousand years to treat a wide range of maladies, attribute its effects to unblocking or removing an excess of qi, or life energy, along key channels referred to as meridians [152].

Results from well-designed studies indicate that auricular acupuncture treatment is not sufficient in efficacy as a stand-alone treatment for opioid dependence. The placebo response rate is substantial, and the body of evidence does not demonstrate the type of qualitative and quantitative rigor needed to validate acupuncture efficacy in the treatment of opioid-addicted patients. Common adverse events from acupuncture include needle pain, fatigue, and bleeding; fainting and syncope are uncommon. Feelings of relaxation are reported by as many as 86% of patients [151]. There is some evidence that differences in efficacy may be influenced by racial physiologic differences among persons of European and Asian descent [151].

A 2016 review of 199 studies found that contradictory results, intergroup differences, and acupuncture placebo effects made it difficult to evaluate the effectiveness of acupuncture for drug addiction treatment [153]. The authors of another review looked at clinical trials of 100-Hz electroacupuncture for detoxification treatment. They found a potential for the treatment to allay opioid-associated depression and anxiety but no effect for opioid craving [154].

Prognosis of Treatment for Opioid Use Disorder

The relapse rate among patients receiving treatment for opioid dependence and other substance abuse is high (25% to 97%), comparable to that of other patients with chronic relapsing conditions, including hypertension and asthma [155]. Many cases of relapse are attributable to treatment noncompliance and lack of lifestyle modification [156].

Duration of agonist replacement therapy is usually recommended as a minimum of one year, and some patients will receive agonist replacement therapy indefinitely. Longer durations of treatment are associated with higher rates of abstinence from illicit opioids [139].

Much remains unknown about patient outcomes following termination of long-term opioid replacement therapy. Some patients aim to achieve total abstinence from all opioids, but little is known about patient characteristics and strategies used among those who remain abstinent. It is likely that at least some of the patients who remain abstinent from all opioids do so with the help of a 12-step support program, such as NA [139].

PREVENTION

Addressing overprescribing of pain medications through improved pain management and prescription monitoring has been one important prevention approach; and as illicit opioids like heroin and imported fentanyl become more prevalent, reducing the supply of those substances through law enforcement efforts is also crucial. But reducing the demand for opioids by addressing the reasons people turn to them and become addicted in the first place is just as vital and fundamental to ensuring that a new drug epidemic does not follow once the opioid crisis is contained [157]. Prevention programs can take many forms, but all in one way or another address these risk factors and/or bolster factors like self-control, peer relationships, or other age-appropriate skills. Because risk factors for drug use are common to other behavioral problems, most prevention interventions do not focus solely on preventing drug use or on preventing a single type of drug use. A wide range of problems can be addressed or averted by addressing core risk or protective factors [157].

CONCLUSION

Opioid analgesic medications can bring substantial relief to patients suffering from pain. However, the inappropriate use, abuse, and diversion of prescription drugs in America, particularly prescription opioids, has increased dramatically in recent years and has been identified as a national public health epidemic. A set of clinical tools, guidelines, and recommendations are now available for prescribers who treat patients with opioids. By implementing these tools, the clinician can effectively address issues related to the clinical management of opioid prescribing, opioid risk management, regulations surrounding the prescribing of opioids, and problematic opioid use by patients. In doing so, healthcare professionals are more likely to achieve a balance between the benefits and risks of opioid prescribing, optimize patient attainment of therapeutic goals, and avoid the risk to patient outcome, public health, and viability of their own practice imposed by deficits in knowledge.

Implicit Bias in Health Care

The role of implicit biases on healthcare outcomes has become a concern, as there is some evidence that implicit biases contribute to health disparities, professionals' attitudes toward and interactions with patients, quality of care, diagnoses, and treatment decisions. This may produce differences in help-seeking, diagnoses, and ultimately treatments and interventions. Implicit biases may also unwittingly produce professional behaviors, attitudes, and interactions that reduce patients' trust and comfort with their provider, leading to earlier termination of visits and/or reduced adherence and follow-up. Disadvantaged groups are marginalized in the healthcare system and vulnerable on multiple levels; health professionals' implicit biases can further exacerbate these existing disadvantages.

Interventions or strategies designed to reduce implicit bias may be categorized as change-based or control-based. Change-based interventions focus on reducing or changing cognitive associations underlying implicit biases. These interventions might include challenging stereotypes. Conversely, control-based interventions involve reducing the effects of the implicit bias on the individual's behaviors. These strategies include increasing awareness of biased thoughts and responses. The two types of interventions are not mutually exclusive and may be used synergistically.

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