Prescription Opioid Misuse, Abuse, and Treatment in the United States: An Update

Kathleen T. Brady, M.D., Ph.D., Jenna L. McCauley, Ph.D., Sudie E. Back, Ph.D.

Objective: Prescription opioid abuse and dependence have escalated rapidly in the United States over the past 20 years, leading to high rates of overdose deaths and a dramatic increase in the number of people seeking treatment for opioid dependence. The authors review the scope of the abuse and overdose epidemic, prescription practices, and the assessment, treatment, and prevention of prescription opioid misuse and dependence.

Method: The authors provide an overview of the literature from 2006 to the present, with the twin goals of highlighting advances in prevention and treatment and identifying remaining gaps in the science.

Results: A number of policy and educational initiatives at the state and federal government level have been undertaken in the past 5 years to help providers and consumers, respectively, prescribe and use opioids more responsibly. Initial reports suggest that diversion and abuse levels have begun to plateau, likely as a result of these initiatives. While there is a large body of research suggesting that opioid substitution coupled with psychosocial interventions is the best treatment option for heroin dependence, there is limited research focusing specifically on the treatment of prescription opioid dependence. In particular, the treatment of chronic pain in individuals with prescription opioid use disorders is underexplored.

Conclusions: While policy and educational initiatives appear to be effective in decreasing prescription opioid abuse and misuse, research focusing on the development and evaluation of treatments specific to prescription opioid dependence and its common comorbidities (e.g., chronic pain, depression) is critically needed.

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Definitions

Several terms are commonly used in the literature to describe prescription opioid use patterns. Regular opioid use, including opioids used in a therapeutic context, is associated with *physical dependence*, characterized by a set of signs and symptoms when drug taking is stopped, and *tolerance*, in which more of the drug is needed to achieve the same intensity of effect. The amount and duration of use associated with physical dependence is variable, but daily use for more than 2–3 weeks is often accompanied by some withdrawal. Being physically dependent does not necessarily mean that an individual has an opioid use disorder, if the individual is taking the medications as prescribed.

Definitions of *abuse* and *misuse* vary, but generally *misuse* of opioids is a broad term that captures any use outside of prescription parameters, including misunderstanding of instructions, self-medication of sleep, mood, or anxiety symptoms, and compulsive use driven by an opioid use disorder. It is important to distinguish between different causes of misuse in order to appropriately address it. *Abuse* is a nonspecific term that can refer to use without a prescription, in a way other than prescribed, or for the experience or feelings elicited. *Diversion* refers to "the transfer of a controlled substance from a lawful to an unlawful channel of distribution or use" (Uniform Controlled Substances Act of 1994, Section 309) and includes both selling and giving to family members or friends for their use. *Pseudoaddiction* is a term applied to situations in which a patient exhibits distress and engages in medication seeking because pain treatment is inadequate. It is best addressed by improving pain control, with or without opioids (1). Patients who are physically dependent on an opioid that was prescribed for pain may continue to use the medication after pain resolution to avoid withdrawal symptoms. This can generally be managed by tapering the opioid.

Thus, the use of DSM criteria in the diagnosis of substance use disorders in individuals receiving opioid analgesics for pain conditions can be complicated because many of the criteria cannot be strictly applied (Table 1). Clinicians must be vigilant in monitoring behavioral criteria specifically associated with opioid use disorders and aberrant use (Table 2) and assessing these criteria within the clinical context.

Scope of the Problem

Since the late 1990s, the prevalence of prescription opioid misuse and abuse has escalated rapidly in the United States (2). Prescription opioids are now one of the most commonly initiated drugs, second only to marijuana, with approximately 1.9 million new initiates per year (3, 4). Epidemiologic data from the 2012 National Survey on Drug Use and Health indicate that 12.5 million Americans reported the abuse of prescription opioids,

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TABLE 1. Applicability of DSM-5 Criteria to Patients Receiving Opioids for Pain

DSM-5 Criteria for Dependence	Medical Use of Opioids for Chronic Pain
Tolerance	Expected with prolonged use
Withdrawal	Expected with prolonged use
Using larger amounts for longer time	Pain may last longer than expected
Wants to quit, not able	Pain can interfere with dose tapering
Lots of time getting, using, recovering from substance use	Criterion can be applied: if opioids are prescribed, should not be spending excessive time procuring
Cravings or urges to use	Distinguish from pain-related urges
Not managing at work, etc.	Distinguish problems related to pain from problems related to opioid use
Continuing to use despite problems in relationships	Criterion can be applied: if pain is adequately treated, relationships should improve
Giving up important activities	Criterion can be applied: if pain is adequately treated, ability to engage in activities should improve
Continuing to use despite danger	Criterion can be applied: if opioids are used as prescribed, should be minimal danger
Using despite physical or psychological problems	Must distinguish from problems related to pain

a significant increase from 4.9 million in 1992 (4). From 2000 to 2010, rates of accidental prescription opioid overdose increased almost fourfold (5) and treatment admissions for prescription opioid dependence increased more than fivefold (6).

In the decades before 1990, physicians were criticized for undertreating pain. In the late 1990s, however, there was a paradigm shift. Pain came to be referred to as the "fifth vital sign," and physicians were encouraged to address and aggressively treat pain. In 2012, the number of prescriptions written for opioids (259 million) equaled the adult population of the United States (4). Pain management is now front and center in the United States as health care providers and policy makers attempt to minimize the negative effects of increased access to prescription opioids while simultaneously ensuring that pain is adequately treated.

TABLE 2. Aberrant Drug-Taking Behaviors in Patients Receiving Opioids for Pain

Clearly Problematic	Potentially Problematic
Selling	Hoarding
Forging prescriptions	Specific type of drug requested
Stealing drugs from others	
Using by nonprescribed route (e.g., injecting or crushing and snorting)	
Doctor shopping	
Repeated losing, running out early	Single loss, running out early
Multiple dosage increases	Single dosage increase

Prescription Opioid Overdose

As noted, rates of unintentional overdose on prescription opioids increased almost fourfold from 2000 to 2010, accounting for more than half of all overdose deaths and exceeding overdose deaths attributed to all other illicit drug categories combined (7). Concomitant use of multiple prescribed and illicit substances is implicated in the majority of overdose deaths (8). Of note, concomitant use of benzodiazepines is the most common factor in prescription opioid-related overdose deaths (9). Male gender, nicotine use, higher prescribed opioid dosages, inappropriate prescribing procedures, and a substance abuse history are associated with risk of opioid-related overdose (8). Methadone use is also linked with a high proportion of overdose deaths (10).

Death from prescription opioid overdose most often results from loss of consciousness and respiratory suppression. Naloxone largely reverses the effects of opioid overdose, including respiratory depression. When administered intramuscularly or intravenously, naloxone has a rapid effect on respiratory depression, within 1 to 2 minutes of administration. Although initial investigations of intranasal naloxone did not support its effectiveness, a recent randomized clinical trial of an intranasal reformulation found that it was as effective as intravenous naloxone in reversing opioid overdose-induced respiratory and CNS depression (11). Intranasal naloxone has the advantage of reducing the risks of needle-stick injury and transmission of blood-borne illnesses, as well as the potential for peer administration of naloxone (12). Many overdose deaths are preventable if symptom-reversing treatment is delivered within an acute time frame; to this end, recent policy efforts extend naloxone access to law enforcement personnel, emergency medical technicians, and other first responders (13).

Prescription Practices

Opioids include natural opioids and man-made congeners that act primarily on three receptors types in the nervous system: mu, kappa, and delta receptors. The mu receptor is primarily responsible for the analgesic and euphoric properties of opioids, and efforts to develop an agent that can produce analgesia without abuse potential have been unsuccessful. Many of the opioid analgesics in use today are full mu agonists (morphine, oxycodone, hydrocodone). Buprenorphine is a partial mu agonist that was approved in 2002 as an office-based treatment for opioid dependence. Because it is a partial agonist, there is less risk of overdose and long-term use is associated with less severe withdrawal symptoms. Opioid antagonists, including naloxone, naltrexone, and nalmefene, bind to opioid receptors without activity and can be used to block or reverse the effects of opioids (for a review, see reference 14).

Opioids comprise many specific agents available in a wide range of formulations. Short-acting orally administered opioids (e.g., immediate-release morphine, hydromorphone, codeine, fentanyl, hydrocodone, and oxycodone) typically have a rapid onset of action (10–60 minutes) and a relatively short duration of action (2–4 hours) and are generally used for acute or breakthrough pain. Extended-release or long-acting opioids have a slower onset of action (30–90 minutes) and a longer duration of action (4–72 hours) and are typically used for chronic pain conditions (15). Providers should not prescribe more than one short-acting opioid concurrently without documented medical justification. Combination products containing an opioid and a nonopioid analgesic are generally used in patients with moderate pain. Using a combination product when dosage escalation is required increases the risk of adverse effects from the nonopioid coanalgesic (e.g., liver damage from acetaminophen), even if an increase of the opioid dosage is appropriate (16). In such cases, using a pure opioid may be preferable. Single-agent formulations are available for codeine, morphine, oxycodone, oxymorphone, hydrocodone, and hydromorphone.

As concern about opioid misuse and abuse has risen, efforts have focused on creating abuse-deterrent and tamper-resistant opioid formulations. A 4:1 formulation of buprenorphine and naloxone designed for sublingual administration, marketed under the name Suboxone, is the most commonly used buprenorphine formulation. Sublingual naloxone will not precipitate withdrawal; however, if Suboxone is taken intravenously, the naloxone will block the euphorigenic effects of buprenorphine and may precipitate withdrawal. Another deterrent formulation incorporates an opioid antagonist into a separate compartment deep within a single capsule, so that crushing the capsule would release the antagonist and neutralize the opioid effect. Another strategy is to modify the physical structure of tablets or incorporate compounds that make it difficult to liquefy, concentrate, or otherwise transform the tablets. In 2014, the Food and Drug Administration (FDA) approved a new extended-release oxycodone/naloxone formulation (Targiniq ER) with abuse-deterrent properties. Transdermal opioid formulations have been perceived in the past as less vulnerable to misuse, but such formulations can be abused.

Efforts to Prevent Opioid Misuse and Abuse

The Office of National Drug Control Policy recently expanded the National Drug Control Strategy to include specific recommendations to enhance efforts to prevent opioid abuse. Recommendations include 1) educating patients and providers about the risks associated with misuse and abuse (e.g., patient-provider treatment agreements); 2) enhancing Prescription Drug Monitoring Program utility and use; 3) increasing proper disposal of prescription drugs to prevent diversion; and 4) addressing key sources of diversion (doctor shopping and "pill mills") through enforcement. In addition, best-practice recommendations from a variety of professional societies recognize the need to balance the benefits of opioids in managing pain with the potential risks conferred, particularly by chronic use. Recommendations support the universal application of risk mitigation strategies such as screening and monitoring assessments, mental health screening, treatment agreements, dosing guidelines, and urine drug screens at regular intervals (17). Continuing medical education, academic detailing, and consultations show promise in supporting risk mitigation strategy implementation (18).

Federal and state legislative efforts also have a significant role in stemming the opioid abuse epidemic. The Drug Enforcement Agency (DEA) and the FDA are the primary federal agencies charged with overseeing the execution of prescription opioid misuse prevention efforts. The DEA imposes penalties for inappropriate prescribing practices, such as jail time, fines, and revocation of licensure, while the FDA requires Risk Evaluation and Mitigation Strategies (REMS) from drug manufacturers. Although REMS are intended to help balance the risk-benefit profile of opioid medications by requiring manufacturers to provide training and education to physicians regarding universal precautions in opioid prescribing, their effectiveness has not been systematically evaluated.

Much of the legislative effort focusing on prescription opioid misuse has been at the state government level, and it varies widely from state to state. Common themes include expansion and mandated use of state-run Prescription Drug Monitoring Programs; extending naloxone access for overdose treatment to law enforcement and emergency first responders; immunity for individuals receiving treatment for overdose; expansion of substance abuse screening and treatment; mandating prescriber education and training in pain management, opioid prescribing, and substance abuse assessment; and increasing "prescription drug take-back" resources (19). Implementation of many of these policies is recent, and few rigorous evaluations have been conducted to examine the effects of these statewide policies. However, increasing evidence supports the effectiveness of several specific policies, including expansion of drug take-back and Prescription Drug Monitoring Programs (20, 21). More broadly, policy changes show promise in enacting and enforcing evidence-supported prescribing practices that reduce risk for abuse and diversion while maintaining or improving the clinical management of pain.

Screening and Assessment

Because it is difficult to predict who will abuse opioid medications, universal risk evaluation is strongly encouraged, which means that all patients, including opioid-naive patients, should be screened for potential risk of abuse using a validated instrument before starting opioid therapy. Positive results from screening should be followed up with a more extensive assessment to gather additional information. All patients receiving opioid therapy, regardless of risk level, should receive education regarding the safe use, storage, and disposal of opioid medications (e.g., take them only as directed, get them from only one provider, do not borrow them from others, do not combine them with alcohol).

TABLE 3. Standardized Screening and Assessment Measures for Use in Opioid Therapy

Measure	Format/Purpose
Screening	
Screener and Opioid Assessment for Patients With Pain (24)	Self-report; used to facilitate assessment and planning for patients being considered for long-term opioid treatment
Opioid Risk Tool (25)	Self-report; used to assess risk of opioid abuse in primary care settings for patients being considered for opioid treatment
Alcohol Use Disorders Identification Test (26)	Self-report; used to identify hazardous and harmful patterns of alcohol consumption
Alcohol, Smoking, and Substance Involvement Screening Test (27)	Self-report; used to detect substance use and related problems in primary and general medical care settings
Drug Abuse Screening Test (28)	Self-report; used to help identify individuals who are abusing drugs
Diagnosis	
Alcohol Use Disorders and Associated Disabilities Interview Schedule (29)	Clinician administered; diagnostic interview
Composite International Diagnostic Interview (30)	Clinician administered; diagnostic interview
Structured Clinical Interview for DSM-IV (31)	Clinician administered; diagnostic interview
Mini-International Neuropsychiatric Interview (32)	Clinician administered; diagnostic interview
Symptom monitoring	
Current Opioid Misuse Measure (33)	Self-report; used to identify whether a patient currently on long-term opioid treatment is exhibiting aberrant behaviors associated with misuse
Addiction Severity Index (34)	Clinician administered; used to assess areas of functioning often affected by substance abuse (e.g., medical, legal, psychiatric, alcohol, drug, social)
Timeline follow-back (35)	Clinician administered; used to monitor amount and frequency of substance use

Factors associated with increased risk of prescription opioid abuse in cross-sectional studies include younger age (18–25 years old), male gender, psychiatric disorders (e.g., depression, bipolar disorder), exposure to violence or sexual assault, a history of substance use disorders (in particular illegal drug use), and a family history of substance use disorder (2, 22). Men are more likely than women to use prescription opioids via alternative routes (e.g., crushing and snorting pills), and women are more likely than men to receive prescriptions for opioids combined with sedatives, an important risk factor for inadvertent overdose (23).

There are several validated screening tools to help providers assess the risk of possible opioid misuse (Table 3). It is critical that all patients be screened prior to initiating opioid therapy. Validated screening measures include the Screener and Opioid Assessment for Patients With Pain (24) and the Opioid Risk Tool (25). The Screener and Opioid Assessment for Patients With Pain is a self-report measure, available in 5-, 14-, or 24-item versions. The 14- and 24-item versions have the strongest sensitivity, specificity, and predictive validity. The Opioid Risk Tool is also a self-report measure, which is brief and easy to use and demonstrates good sensitivity and specificity. Thus, both of these instruments are useful to help identify patients being considered for opioid therapy who may be at risk for misuse or abuse of opioid medications. Positive screening alone is insufficient to rule out opioid therapy, and a positive screening result should be followed up with a more comprehensive assessment, including urine drug screen tests and a clinical evaluation to determine the safety and risk-benefit ratio of opioid therapy.

Once opioid therapy has been started, it is important to monitor the patient during treatment. The Current Opioid Misuse Measure (33) is a self-report measure that can facilitate the monitoring of patients on opioid therapy. It takes less than 10 minutes to complete and includes 17 items that evaluate six key issues: signs and symptoms of intoxication, emotional volatility, poor response to medications, substance use disorders, health care use patterns, and problematic medication behavior. For patients with a prior history of opioid use but no history of misuse or abuse, providers should screen for factors suggesting an increase in risk, especially since the last time the patient received a prescription for an opioid (e.g., recent alcohol or drug use disorders, mental health problems), before reinstating opioid therapy.

For patients with a history of opioid misuse, thoughtful assessment and planning are necessary. Assessment should include a thorough history of prescription opioid use (e.g., age at onset, reasons for use, source, route of administration, reasons for escalation), other opioid use (e.g., heroin, injection), treatment history and outcome, other substance use including other prescription medications (e.g., benzodiazepines), psychiatric illnesses, and medical conditions. Evaluation of other substance use is critical given the increased risks of overdose and death associated with concomitant substance use, in particular benzodiazepines and alcohol (5). Assessment of family members and caretakers, as well as consultations with mental health professionals and substance use disorder specialists, may also be needed. A thorough evaluation will help providers and patients determine the best approach to treatment, which may involve other forms of treatment or interventions (e.g., nonpharmacologic treatment approaches for pain, cognitive-behavioral therapy for a psychiatric disorder) prior to considering reinstating

opioid therapy. If the patient does resume opioid therapy, consider more frequent monitoring, pill counts, checking the Prescription Drug Monitoring Program at each visit and with each refill, using a decreased amount and supply of medication, regular engagement of mental health professionals or social workers, and incorporation of family members.

All patients who are started on opioid therapy should be monitored on a regular basis. Particular attention should be given to the escalation of opioid use and any negative impact on the patient's ability to function across multiple domains of life (e.g., occupational, social, family). See Table 3 for examples of standardized assessments that may be helpful in monitoring for aberrant behaviors during ongoing opioid therapy (24–35).

Treatment of Prescription Opioid Use Disorders

Although prescription opioid use disorders are approximately four times more prevalent than heroin use disorders, treatment outcome research specific to prescription opioid use disorders is limited, and the extent to which treatments developed for heroin dependence can be successfully generalized to prescription opioid dependence remains unclear (36). In the absence of protocols specific to prescription opioid use disorders, most treatment facilities defer to the evidence base amassed regarding treatment options for opioid use disorders more broadly. Evidence-based treatment of opioid use disorders has been reviewed at length elsewhere (e.g., 37) and will be discussed only briefly here, allowing for more in-depth focus on treatment outcome trials specific to prescription opioid use disorders.

Treatment for opioid use disorders typically involves medically supervised detoxification (38) followed by maintenance with opioid substitution therapies (39). Opioid substitution therapy involves administration of controlled amounts of longer-acting opioids with less euphoric effects in an effort to reduce craving and prevent withdrawal symptoms. Opioid substitution therapy often involves long-term, or even lifetime, use of medication (40). The two most common substitution therapies are methadone and buprenorphine. Approximately one-quarter of individuals with opioid use disorders have received methadone maintenance therapy, making it the most commonly used replacement therapy for opioid use disorders.

Effectiveness rates for methadone maintenance therapy range from 20% to 70%, and outcomes are dose related, with individual variability in the effective dose. Lower dosages (20–40 mg/day) are effective at suppressing opioid withdrawal but may not sufficiently decrease craving or block the effects of other opioids. Maintenance dosages are generally in the range of 70–120 mg/day, although some patients may require more than 120 mg/day for optimal therapeutic response. Methadone is useful for suppressing withdrawal and blocking the effects of other opioids, and methadone maintenance therapy provides a context in which prosocial activities and health issues can be addressed. Studies have shown that methadone maintenance therapy enhances treatment retention, decreases illicit opioid and other drug use, and is associated with decreased criminal activity (14), although other studies have not reported any impact of methadone on criminal activity (37).

In 2002, the FDA approved office-based administration of buprenorphine, and by 2012, 51% of opioid treatment programs (www.buprenorphine.samhsa.gov) offered buprenorphine (4). Because it is a partial mu agonist, buprenorphine is associated with less euphoria and sedating effects than methadone and has been shown to decrease withdrawal, hospital admissions, morbidity, and mortality among patients with opioid use disorders (41). Studies suggest that buprenorphine outcomes (at 8 mg/day sublingually) are superior to placebo, and similar to daily doses of 50–60 mg per day of methadone (42). Similar to methadone maintenance therapy, buprenorphine therapy can be maintained for years.

Long-term (or lifetime) replacement therapy is not an attractive option for some individuals with opioid use disorders. In these cases, a substitution therapy (usually buprenorphine or Suboxone) is gradually tapered and eventually replaced with naltrexone to promote sustained opioid abstinence (43). Naltrexone is an opioid antagonist that blocks the euphorigenic effects of opioids. Whereas the effectiveness of naltrexone has been historically hampered by low adherence rates, injection and implant options, recently approved by the FDA, showed promising results in a recent trial (44). Naltrexone is easy to administer, does not induce tolerance, and is not addictive. However, because naltrexone diminishes opioid tolerance, it can increase the risk of overdose in individuals who return to illicit drug use. Overdose deaths associated with oral naltrexone are 3–7 times higher than those associated with methadone maintenance therapy (45).

Treatment Outcomes Specific to Prescription Opioid Use Disorders. Recent results from the Starting Treatment With Agonist Replacement Therapies (START) study, a multisite trial that included individuals with both intravenous and prescription opioid use disorders (46), suggested that prescription opioid analgesic-only users may be more likely to stay in treatment longer and achieve better outcomes than their counterparts with histories of heroin or other injection use. The availability of buprenorphine through office-based practice rather than specialized clinics, coupled with the ability to prescribe a 30-day supply as opposed to daily clinic administration, led to the hypothesis that buprenorphine may be the more attractive treatment for patients. Contrary to this initial hypothesis, START study results indicated no significant advantage for Suboxone over methadone maintenance therapy with respect to opioid use outcomes at up to 24 weeks of active treatment, suggesting that either approach presents a viable treatment option for prescription opioid use disorders.

Preliminary evidence also suggests that individuals with prescription opioid use disorders may initiate and maintain abstinence with a brief but intensive outpatient Suboxone

taper, followed by adherence to long-term naltrexone (47). Although this option for tapered outpatient management may be particularly appealing in rural areas where access to methadone maintenance therapy programs is limited (48), evidence supporting the effectiveness of this approach is inconclusive, and further evaluation is needed (49).

The Prescription Opioid Addiction Treatment Study (50), the largest existing randomized controlled trial of treatment for prescription opioid use disorders, examined differential intensities and combinations of counseling and buprenorphine-naloxone treatment for patients with DSM-IV dependence on opioid analgesics. Phase 1 of this multisite trial consisted of induction, a 2-week medication stabilization period, a 2-week medication taper, and an 8-week postmedication follow-up. Individuals who relapsed during phase 1 were transitioned to phase 2, which consisted of a 12-week medication stabilization period, a 4-week medication taper, and an 8-week posttreatment follow-up. Across each phase, participants were randomized to either standard medical management or standard medical management plus individual opioid drug counseling. The primary outcome was abstinence from opioids during the final 4 weeks of buprenorphine-naloxone stabilization (weeks 9–12), based on urine drug screening and self-report.

Overall, treatment success rates were 7% in phase 1 and 49% in phase 2, suggesting that longer medication treatment and a slower medication taper were associated with better outcomes (50). Treatment outcomes were predicted by medication response at 2 weeks: abstinence during the initial 2 weeks of treatment was moderately predictive of successful treatment outcomes, and opioid use during the initial 2 weeks of treatment was a strong predictor of unsuccessful treatment outcomes (51). Furthermore, heterogeneity in response to stabilization and taper predicted time to first use, such that the following groups evinced the shortest to longest period of abstinence: 1) high levels of craving and withdrawal, 2) intermediate levels of craving and withdrawal, 3) high initial craving with low craving and withdrawal trajectories, and 4) low initial craving with low craving and withdrawal trajectories (52).

Treatment outcomes for the Prescription Opioid Addiction Treatment Study have been reported for 18 months (53) and 42 month (54), and were notably improved in comparison to initial 12-week outcomes. Nearly one-third (31.7%) of treatment completers were abstinent and no longer on agonist treatment, and 29.4% continued to receive agonist therapy but met no criteria for a current prescription opioid use disorder. Conversely, nearly one-third (31.4%) reported illicit opioid use in the absence of agonist therapy and 7.5% were using opioids illicitly while still receiving agonist therapy. A small but important subsegment of individuals got worse during the course of treatment and follow-up: 8% reported first-time heroin use and 10% reported first-time injection use. Heroin use and pain severity at baseline were associated with poorer treatment outcomes. Engagement with agonist therapy was associated with better long-term outcomes.

Critical Evidence Gaps in Treatment of Prescription Opioid Use Disorders. The literature pertaining to the treatment of patients presenting with a primary prescription opioid use disorder, particularly those with a chronic pain condition that led to initial use of opioids, is sparse, preventing concrete conclusions regarding the comparative effectiveness of existing treatment options beyond those drawn from research with broader opioid use disorder samples. The development or adaptation of treatment protocols addressing patients with prescription opioid use disorders is a critical need in reducing the public health burden associated with the current epidemic.

Additionally, further research is warranted on treatment tailored for special populations of individuals with prescription opioid use disorders previously identified in the broader opioid use disorder population, including polysubstance abusers, pregnant women, and HIV-positive individuals. Consistent with treatment approaches to opioid use disorders, patients with active use of other sedative-hypnotics (alcohol, benzodiazepines, and barbiturates) are typically detoxified and required to discontinue substance use prior to initiation of treatment. Because of potential medication interactions, buprenorphine is used with caution and monitored closely in patients with HIV on antiretroviral therapy. Although Suboxone is not recommended for pregnant women, buprenorphine monotherapy is typically recommended and has demonstrated better short-term and potentially long-term outcomes than methadone maintenance therapy for this population (55). No studies to date have addressed the general application of these clinical approaches to individuals with only a prescription opioid use disorder.

Finally, the treatment literature on opioid use disorders has traditionally indicated that integrated, multifaceted treatments incorporating both pharmacotherapy and psychosocial interventions have a higher likelihood of success than pharmacotherapy alone (39). Specifically, contingency management protocols have shown promise in enhancing retention and compliance among patients with opioid use disorders (56). However, recent research specific to prescription opioid use disorders suggested no overall additional benefit from counseling (50), although subpopulations with more severe opioid use that included heroin may receive added benefit when engaged in counseling coupled with medical management (57). At present, the data are insufficient to provide guidance on the type (or inclusion) of psychosocial treatment—contingency management, relapse prevention, support groups like Narcotics Anonymous—that might be most effectively partnered with opioid substitution therapy. Identification of treatment combinations that work best for specific patient subgroups is an important area for future research.

Treatment of Pain in Substance-Dependent Individuals

The treatment of pain in individuals with addiction disorders does not differ significantly from the treatment of pain in nonaddicted individuals. Individuals with substance use

disorders are at greater risk than the general public for accidents and injuries associated with pain (58), and untreated pain can be a significant trigger for relapse (59). The goals of treatment are the reduction of pain and restoration of function. In the management of moderate to severe acute pain, opioids are generally the mainstay of treatment in addicted or nonaddicted individuals. Scheduled administration of opioids is preferred to as-needed administration in individuals with addictive disorders, as it provides several advantages. If the patient needs to ask for pain medication, this may be misconstrued as drug-seeking behavior. In addition, when drug administration is time rather than symptom dependent, reinforcement of pain symptoms is minimized. Individuals on methadone maintenance therapy or those who are physically dependent on other opioids should have their baseline opioid requirements met in addition to the medication provided for pain treatment. When possible, patients on methadone maintenance therapy should receive a different opioid medication for the control of acute pain or have additional methadone prescribed on a three- or four-times-daily basis. The management of patients on buprenorphine who develop an acute pain condition is somewhat more complex, with less data and clinical experience available for guidance. Although buprenorphine is an effective analgesic, it does not have the potency of a full-agonist opioid. Options include increasing the dosage of buprenorphine and giving it in divided doses throughout the day or adding a full-agonist opioid to the regimen for the period of acute pain, although the efficacy of a full agonist in the face of receptor occupancy by buprenorphine is not clear. A third option is to discontinue buprenorphine and switch temporarily to a full-agonist opioid while acute pain treatment is needed. When the acute pain subsides, the patient can be reinducted on buprenorphine.

In the treatment of chronic pain, treatment goals are approached initially through the use of nonpharmacological strategies, such as a transcutaneous electrical nerve stimulation (TENS) unit, peripheral nerve blocks, or trigger point injections. The mainstay of medication treatment for chronic, nonmalignant pain includes nonsteroidal anti-inflammatory drugs, tricyclic antidepressants, and anticonvulsants. Anticonvulsants (pregabalin) and antidepressant agents (duloxetine) have recently received FDA approval for specific pain syndromes. There is no nationally accepted consensus concerning chronic pain management, but published consensus statements emphasize the importance of using a standardized approach so that decisions about the use of opioids and dosage increases can be clearly justified. Clinicians should be aware that long-term opioid use may be associated with the development of abnormal sensitivity to pain (i.e., hyperalgesia), which manifests clinically as needing increasing dosages of opioids to maintain the same level of analgesia. However, dosage escalation should be approached with caution, and ongoing assessment to determine whether the increased dosing is meeting the goals of treatment (decreased pain, improved functionality) is essential. Failure to meet goals requires re-evaluation and change in treatment plan.

Medication agreements, written statements that reinforce the patient's responsibility and clarify the boundaries of treatment, may be useful in the management of pain, as they can help in avoiding misunderstandings and clarifying decision points related to opioid prescribing (16). Even when medications, including opioids, are deemed necessary in the treatment of chronic pain syndromes, the treatment plan should be multidimensional. Specifically, it should include a careful history of the pain problem, factors that contribute to the patient's pain and distress, and a plan for dealing with each of these contributing factors. The treatment plan may include the physical treatments of pain mentioned previously (i.e., a TENS unit, nerve blocks), as well as behavioral interventions, such as relaxation training and biofeedback. While the majority of chronic pain patients achieve relief through multimodal approaches that do not include opioids, the use of long-term opioids as one component in the treatment of chronic pain is considered a reasonable approach when other treatment regimens have failed. For most patients, a trial period with the use of coordinated alternative treatments should be tried before long-term opioid therapy is used. When opioids are used, it is important to document their benefit by improvement in functional status.

Conclusions and Recommendations

The prevalence of prescription opioid abuse and misuse has escalated rapidly in the United States over the past 20 years, leading to dramatic increases in overdose deaths and individuals seeking treatment for opioid use disorders. In response to this public health crisis, a number of policy and educational initiatives have been implemented to help providers and patients, respectively, prescribe and use opioids more responsibly. While the effectiveness of these initiatives is currently under evaluation, initial reports suggest that diversion and abuse rates have plateaued, likely a result of these initiatives as well as a shift in FDA and best-practice recommendations indicating that extended-release or long-acting opioids should be reserved for the treatment of severe pain (60). Treatment research on opioid use disorders was largely focused on intravenous heroin use until 5–10 years ago, so studies focusing specifically on prescription opioid use disorders remain limited. Studies focusing primarily on heroin suggest that replacement therapies, coupled with psychosocial treatment, are the best treatment option, although treatment access remains an issue and treatment utilization rates are low. Additional research focusing on the development and evaluation of treatments specific to prescription opioid use disorders and their common comorbidities (e.g., chronic pain, depression) are critically needed.

AUTHOR AND ARTICLE INFORMATION

From the Addiction Sciences Division, Institute of Psychiatry and Behavioral Sciences, Medical University of South Carolina, Charleston; and the Ralph H. Johnson Veterans Affairs Medical Center, Charleston.

Address correspondence to Dr. Brady (bradyk@musc.edu).

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