Chronic Pain Management in Patients With Substance Use Disorders

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**ABSTRACT**

**Purpose:** To review the evidence and provide a practical guide for the management of chronic pain among patients with substance use disorders.

**Epidemiology:** Chronic pain affects between 24% and 67% of patients with substance use disorders, and is frequently undertreated.

**Review Summary:** The approach to the patient with chronic pain and a prior or active substance use disorder begins with a thorough assessment of the severity and history of past treatments of both conditions, and the presence of psychiatric disorders. Patients benefit the most from combinations of pharmacologic agents, ranging from nonsteroidal anti-inflammatory drugs to antidepressants, neuroleptics, and opioids if needed. Nonpharmacologic interventions play an adjunctive role. When using opioid analgesics, initiating a treatment agreement provides a framework within which opioids can be prescribed in a safe and effective manner. Aberrant drug-taking behavior should be assessed fully as it may signify prescription medication abuse, poorly treated pain, or worsening mental health.

**Type of Available Evidence:** Consensus statements and guidelines from specialty organizations, including the American Pain Society, the American Society of Addiction Medicine, and the American Academy of Pain Medicine; unstructured reviews; cross-sectional surveys; prospective cohort studies; randomized trials; meta-analyses.

**Grade of Available Evidence:** Poor to fair.

**Conclusion:** Although more extensive, high-quality evidence is needed to help guide chronic pain management in patients with past or current substance use, physicians can still deliver effective, appropriate care to this group if they adopt a systematic, well thought out approach that takes into consideration our current understanding of the complex interplay between pain and addiction. (Adv Stud Med. 2006;6(3):111-123)

Managing chronic pain often is challenging for primary care physicians, but it can become even more so when patients also have a history of substance abuse or an active addiction. Medical school and residency curricula prepare physicians poorly for the management of these complicated patients. Little guidance has existed for primary care physicians on how to appropriately treat pain in patients with substance use disorders. Pain medicine specialists and addiction treatment providers commonly care for patients in their own separate spheres without much communication or collaboration. The clinical approach to chronic pain management in substance users has been complicated by confusing and often misunderstood terminology used in pain management and addiction medicine. In addition, many state medical boards have not considered the use of opioid analgesics in patients with substance use disorders to fall within the scope of acceptable medical practice.
However, more recent understanding of the interplay between addiction and pain calls into question this artificial separation. In 1996 the Pain Management and Chemical Dependency Working Group, consisting of national pain medicine and addiction experts, sponsored a symposium focusing on the overlap between pain and addiction. Subsequently, the American Pain Society (APS) and the American Academy of Pain Medicine (AAPM) issued a joint statement supporting adequate pain treatment, with opioids if indicated, even in patients with substance abuse. The American Society for Addiction Medicine (ASAM) has provided full-day sessions entitled “Pain and Addiction: Common Threads” at its annual meetings, and is a key player in a liaison committee on pain and addiction along with the APS and the AAPM.

To clarify the clinical approach to chronic pain treatment, experts have replaced common, ill-defined terms such as “drug-seeking” with more specific language such as “aberrant drug-taking behaviors” to describe ways patients behave in efforts to obtain controlled substances (Figure 1). In addition, they acknowledge that the current combinations of physical and psychologic criteria used to define substance dependence may not be appropriate to define addiction to prescribed analgesics (prescription medication abuse). Physical dependence—manifested by withdrawal upon attempts to cut down use and tolerance, a need to increase the dose to obtain the original effect—is a predictable physiologic consequence of long-term, continuous exposure to alcohol and many drugs, including opioids, whether these are prescribed or illicitly obtained. Physical dependence in and of itself does not indicate true psychologic dependence or addiction.

To emphasize the psychologic characteristics of prescription medication abuse, the ASAM has outlined the “Four Cs” as more useful criteria: loss of Control over the use of medications; Compulsive use of medications; Continued use despite harm; and drug Cravings.

Although pain and addiction medicine specialists are forging new relationships and common language in the care of patients with chronic pain and substance use disorders, primary care physicians still provide treatment to the majority of patients with these comorbid conditions. There simply are not enough subspecialists currently trained to meet treatment needs. Appropriate management of chronic pain in patients with past or current substance use disorders demands that primary care physicians understand the nature and language of both chronic pain and addiction.

**Prevalence of Chronic Pain in Addicted Populations**

As defined by the International Association on Studies in Pain, chronic pain is pain that either lasts longer than 3 months or that persists beyond what would be normally expected from healing after tissue injury (typically felt to be 3 months). Although researchers suggest that the prevalence of chronic pain among individuals with substance use disorders is at least as high as those for the general population, less empiric evidence focuses specifically on those with addictions. Epidemiologic studies in this group are difficult to conduct. The stigma of addiction and the chaotic lives of those with active substance abuse make recruitment, follow-up, and tracking of study participants often inconsistent and costly.

Therefore, the majority of the studies investigating the prevalence of chronic pain among those with past or current substance abuse focus on certain subgroups of people, such as individuals infected with HIV or patients in treatment, particularly those on methadone maintenance. The literature is further hampered by existing reports that define chronic pain according to varying lengths of time, making comparisons across studies difficult.

Despite these limitations, current evidence supports the hypothesis that the prevalence of persistent pain among those with addictions is high. For example, a small study by Anand et al noted that, among 14 substance-using, HIV-positive patients referred to an inpatient pain service, 50% described pain of more than 6 months’ duration. In a prospective cohort study of HIV-positive outpatients, Breitbart et al found that 67% of the 270 participants with active or prior drug use reported persistent or frequent pain.

Two frequently cited cross-sectional surveys suggest that, among methadone-maintained patients, the prevalence of chronic pain ranges from 37% to 61%. Similarly, Trafton et al reported that 52% of 228 treatment-seeking, opioid-dependent veterans complained of moderate to very severe pain lasting more than 30 days. Finally, Mertens et al noted increased odds of 3 pain-related chronic conditions—lower back pain (odds ratio [OR] 2.07, 95% confidence interval [CI], 1.59–2.70), headache (OR 2.56, 95% CI, 1.89–3.46), and arthritis (OR 2.97, 95% CI, 1.83–4.82)—among patients in a health maintenance organization entering drug/alcohol treatment compared with matched controls without a substance use disorder.

In comparison, estimates of chronic pain in non-substance-abusing individuals seen in primary care settings range between 5% and 45%. One extensive review suggests a population prevalence of chronic pain of about 10%.
undertreated. In a study of ambulatory patients with AIDS, only 44% of those with active or treated addiction reported adequate treatment of pain, and current or past drug use significantly predicted severe under-treatment of persistent pain (OR 1.8 [P = .04]).

Multiple, interrelated factors predispose to the under-treatment of chronic pain among patients with active or past substance abuse. For ease of discussion, these factors often are separated into different categories: 1) patient-level; 2) physician-level; and 3) system level.

**Patient-Level Factors**

Patients with addiction are acutely aware of the societal stigma that often follows them even into the healthcare system. Karasz et al found that many methadone-maintained patients did not discuss their pain with physicians because of the belief that their providers would not believe them and would label them as drug-seeking. Inpatients interviewed for a qualitative study reported feeling that even seeking medical care in itself was seen as drug-seeking by healthcare providers and would lead to mistreatment. In fact, patients with histories of substance use disorders often do not want strong medications for pain, such as opioids, for fear of triggering a relapse.

**Physician-Level Factors**

Although recent national attention to pain has heightened physician awareness of the importance of adequate pain treatment, many aspects of this practice, particularly the long-term prescribing of opioid medications, continue to engender discomfort on the part of primary care providers. Physicians may not prescribe effective opioid analgesia to many patients because of fears of adverse side effects, iatrogenic addiction, and/or prescription drug diversion. This tendency to undermedicate patients with opioid analgesics has been termed “opiophobia” and is exaggerated when physicians treat patients who have a known history of or active substance use disorder.

The mistrust that patients with addiction and chronic pain have of healthcare providers often is mirrored by negative attitudes that physicians hold toward this group. Extensive surveys of physicians at all levels of training demonstrate that many providers do not feel comfortable caring for addicted patients, do not like working with patients who have substance use disorders, and generally do not find interactions with these patients rewarding. Primary care physicians often express concern that patients with substance use disorders exaggerate their pain symptoms to obtain opioids. These perceptions may cloud physicians’ approaches to complaints of pain from such patients.

**System-Level Factors**

Criminal and civil suits against physicians for both overprescribing opioids and undertreating pain have heightened physicians’ concerns about managing chronic pain in general. Close scrutiny by the Drug Enforcement Administration, restrictive state policies regarding the prescribing of controlled substances to those with addiction, and controversy in the medical literature over the effectiveness of long-term opioids for chronic non-cancer-related pain all add to the confusion. When considering patients with substance use disorders and chronic pain, fear of opioid medications overshadows much of the discussion on appropriate pain management in this group.

It is important to recognize, however, that the regulatory environment for the use of controlled substances for pain in patients with substance use disorders is slowly improving. There is a growing understanding of the critical psychologic nature of addiction, and recognition of the importance of adequate pain treatment that may require prescription opioids in those with past or active substance abuse.

In 2004 the Federation of State Medical Boards published a revised policy and guideline on the use of controlled substances in the treatment of pain, “to alleviate physician uncertainty and to encourage better pain management.” Several states have adopted or amended Intractable Pain Treatment Acts that recognize the legitimate use of controlled substances in the treatment of chronic pain, and provide legal protection for doctors who appropriately do so.

**Clinical Presentation, Natural History, and Diagnostic Considerations**

**Clinical Presentation and Natural History**

A biopsychosocial model predominantly underpins our current understanding of both chronic pain and addiction, and includes biologic, psychologic, social/interpersonal, and spiritual domains, with multiple contributors that cut across each of these areas. To date, researchers have focused on a few areas to understand how the presence of substance abuse affects an individual’s experience of chronic pain.

Studies describe different types of chronic pain, including neuropathic, myofascial, and nociceptive, among both active and past substance users. In addition, investigators estimate that 19% to 65% of addictive disorders coexist with a mental health condition such as major depression, generalized anxiety, and antisocial or borderline personality disorder. Between 80% and 90% of patients who are actively using drugs may exhibit substance-induced symptoms of a mental health disorder that may resolve within a week of abstinence. Research also shows that the presence of depression exacerbates chronic pain and complicates its treatment. In patients with both chronic pain and a substance use disorder, a comorbid mental
health condition can be particularly detrimental.

Biochemically, the clinical conditions of pain and addiction are related phenomena. Forty-one years ago, Martin and Inglis observed that patients with opioid dependence self-medicate “an abnormally low tolerance for painful stimuli.” Opioids, whether administered with analgesic or addictive intent, activate opiate receptors in the locus coeruleus and amygdala, which provide both analgesia and reward.

A less well understood area, however, is the difference in pain perception between substance-abusing and nonaddicted populations. In a small study, Breitbart et al reported that descriptions of pain experiences did not differ between addicted and non-drug-using HIV-positive individuals with pain. In contrast, Savage and Schofferman found almost a decade ago that persons with addiction and pain have a “syndrome of pain facilitation.” In these patients, subtle withdrawal syndromes, intoxication, withdrawal-related sympathetic nervous system arousal, sleep disturbances, and affective changes worsen pain.

Supporting a negative effect of addiction on pain tolerance, patients who abuse stimulants or opioids are less tolerant of pain than are their peers in remission and those without histories of substance abuse. Hyperalgesia, or increased pain sensitivity, also may develop in patients maintained on methadone or other long-term opioids. A series of studies employing both observational and experimental designs found that methadone-maintained patients had much lower baseline pain thresholds compared to non-substance-using controls when their hands were submerged in a tank of freezing water.

Animal research suggests that pain intolerance may actually precede substance abuse—specifically opioid dependence. Experiments using inbred mouse strains demonstrate that alterations in the mu opioid receptor gene may account for low pain tolerance and high levels of opioid reinforcement in these animals. Human mu opioid receptor gene polymorphisms also have been found in studies of opioid-dependent patients.

From this area of research, it is becoming evident that patients with substance use disorders have a lower tolerance to pain. Further work is needed to clarify how much of this decreased pain tolerance is a result of neurobiologic changes from chronic drug use versus a genetically mediated innate lower pain tolerance that infers a higher risk for developing addiction.

**Diagnostic Considerations: Assessment**

Because of the complex interplay between addiction and chronic pain, a comprehensive clinical approach to patients with these disorders is needed. This begins with a thorough assessment of the severity of chronic pain and substance abuse, keeping in mind that multiple domains may impact a patient’s experience of these disorders. Whereas a number of clinical pain assessment measures exist, none have specifically been validated in addicted populations, where anxiety, fear, past experiences, and other psychologic elements may impact pain ratings. Simple scales such as the Visual Analogue Scale or the faces diagrams provide estimates of an individual’s intensity of pain cross-sectionally and can be used longitudinally to measure the impact of interventions targeting pain. On a 10-point scale, mild pain typically is considered equivalent to a self-reported level of 1 to 3, moderate pain is in the range of 4 to 7, and severe pain is anything above 7.

To understand the impact of chronic pain on function, measures such as the McGill Pain Questionnaire and the Brief Pain Inventory can be used. In addition, physicians should obtain information and results from prior pain evaluations, including imaging and other testing, treatments tried, past psychiatric therapy, and how pain and functional abilities responded to these interventions.

Physicians also should obtain a comprehensive substance abuse history, including drugs of use, quantity, frequency, route of administration, most recent use, overall duration of use, impact of substance use on life and function, past treatments and their effectiveness, and, if still actively using, the patient’s current level of interest in treatment. For substance use disorders, several validated assessment tools applicable to clinical practice exist, such as the Michigan Alcohol Screening Test, and Alcohol Use Disorders Identification Test for alcohol abuse/dependence. A few have been tested in drug-dependent populations, as well.

For patients in substance abuse treatment, physicians should assess the type and frequency of addiction counseling they receive as research shows that counseling has significant positive effects on substance abuse outcomes, particularly when combined with pharmacologic therapy. If patients are receiving disulfiram or naltrexone for alcohol dependence, providers must counsel them about the risks and possible medication interactions associated with these agents.

**Treatment Considerations for Chronic Pain in Patients With Substance Use Disorders**

**Trust in the Patient-Doctor Relationship**

Establishing effective rapport and trust is crucial to any effective physician-patient relationship. This is particularly true when the patient with chronic pain has a previous history of or active addiction. Patients often present to primary care physicians with negative past experiences in the healthcare system, particularly as related to treatment of pain. Some physicians refuse to refill opioid analgesics for new patients if a dif-
The Multidisciplinary Team

goals of treatment and the multidisciplinary team

The overall goals of chronic pain treatment include minimizing pain and maximizing function. Because recent work shows that minimizing pain can occur in the absence of maximizing function and vice versa, chronic pain experts currently emphasize improvement of function as a primary treatment goal.29,75 In addition, parameters spelled out in treatment plans aid in maintaining a consistent structure of care that many patients with substance use disorders have infrequently had in their lives. If controlled substances, such as opioids, are used, separate written agreements or contracts also ensure that both physician and patient agree to common expectations as to how the medications will be prescribed and what the consequences will be for aberrant drug-taking behavior.

TREATMENT OPTIONS FOR CHRONIC PAIN IN PATIENTS WITH SUBSTANCE USE DISORDERS

Nonpharmacologic Therapies

In conjunction with medications, patients with chronic pain and a past or current substance use disorder may benefit from nonpharmacologic interventions. Although many modalities exist, few have been rigorously tested; particularly in patients with comorbid substance use disorders.

Acupuncture is one complementary therapy that has been systematically studied for the treatment of conditions including addiction, fibromyalgia, and low back pain.87-89 In 1998 the National Institutes of Health (NIH) convened a multi-institute consensus development conference on the topic of needle acupuncture90 and found that, when combined with clinical experience, there was enough reasonable evidence to promote this therapeutic option for postoperative dental pain and for fibromyalgia. Although the data are less convincing for addiction, low back pain, headache, and osteoarthritis, the committee felt that needle acupuncture would be a reasonable adjunctive treatment for these conditions given its low risk profile for adverse side effects. Access to licensed acupuncturists has been limited for many individuals with chronic pain and addiction, however, because it is not often covered by insurance. Before advocating its widespread use, numerous researchers, including the NIH consensus group,90 have called for more research to better elucidate the benefits of acupuncture as reviews of existing studies have found mixed results.90,91

Numerous systematic reviews of physical therapy techniques, including exercise, transcutaneous electrical nerve stimulation, and spinal cord stimulation for the treatment of chronic pain demonstrate slight to moderate efficacy in improving pain, and function.
when provided as the main treatment modality. The majority of authors concluded, though, that the size and quality of original studies is generally poor to fair and recommended larger trials for a more definitive assessment of efficacy. Because physical therapy carries with it relatively few adverse side effects and may provide some benefit, pain experts recommend incorporating these techniques as part of a comprehensive treatment plan.

Other nonpharmacologic therapies for chronic pain that have undergone some study include massage therapy, hydrotherapy, yoga, relaxation techniques, and cognitive-behavioral therapy. Systematic reviews reveal a paucity of well-designed randomized trials that have adequate sample sizes and use standard definitions of chronic pain and uniform outcome measures. More recent studies of back pain appear to be of better quality, and suggest that massage therapy has benefits for patients with chronic low back pain—even over acupuncture.

**Pharmacologic Therapies**

**Nonopioid Agents.** The World Health Organization’s pain treatment ladder and guidelines, such as those from the American Pain Society, outline helpful principles for pharmacologic pain treatment that are applicable to patients with addictions. Therapy should begin with agents that target a patient’s particular type of pain and, often, combinations of medications are required. Initial choices, especially for mild to moderate pain, include nonsteroidal anti-inflammatory agents, acetaminophen, muscle relaxants, local anesthetics, antidepressants, and neuroleptics. In systematic reviews, the latter 2 classes of medications have shown particular efficacy in the treatment of neuropathic pain. For moderate to severe pain, medications should be taken on a round-the-clock basis, rather than as-needed. Patients should have frequent follow-up to assess the effectiveness of treatment. If, after an adequate trial, current therapies are not improving set goals, a change in interventions should occur.

**Opioids.** Given the nature of addiction, the challenge of chronic pain, and societal and provider fears about opioids, the question often asked is: “are opioids indicated for chronic pain in patients with addictive disorders, and if so, when?” This question has plagued physicians for many years, and controversy continues. The majority of addiction and pain medicine specialists now agree that patients with substance use disorders should receive opioids as treatment for chronic pain under specific circumstances: 1) when pain is moderate to severe; 2) when pain has a significant impact on function and quality of life; 3) when nonopioids have been tried and failed; and 4) the patient agrees to have opioid use closely monitored.

When opioids are chosen as part of a treatment regimen for chronic pain, guidelines recommend use of long-acting opioids, such as sustained-release morphine or oxycodone or fentanyl patches, over short-acting opioids, such as immediate-release preparations of morphine or oxycodone. Short-acting opioids should be reserved for breakthrough pain. Neurobiologically, short-acting opioids may have a higher addictive potential because of their faster onset of action. It is important to note, however, that all of the long-acting preparations currently available have abuse potential when the tablets or patches are altered, as this shortens the drug’s onset of action.

Not all chronic pain is opioid responsive. To determine pain’s responsiveness to opioid analgesics, doses must balance efficacy—improved pain and function—with no or limited adverse effects such as sedation. Particular types of chronic pain, such as myofascial and nociceptive pain, are considered more opioid responsive in that dose for dose, higher levels of analgesia with fewer side effects may be achieved than in patients with neuropathic pain. However, it is important to keep in mind that some patients exhibit a behavior termed pseudo-opioid resistance. This refers to instances in which patients with adequate pain control continue to complain of persistent severe pain because they fear that reported improvements in pain would lead to less care from the physician, and/or a reduction in current effective opioid analgesic dose.

For patients with opioid dependence being treated with methadone maintenance therapy, higher doses of opioid analgesics may be necessary for adequate pain control. As documented by Doverty and colleagues, patients on methadone maintenance typically develop tolerance to their daily methadone dose with subsequent cross-tolerance to standard doses and duration of action of opioid analgesics used for pain management. In addition, although methadone itself is a potent analgesic, its duration of action for analgesia, 4 to 8 hours, is substantially shorter than its suppression of opioid withdrawal, which averages 24 to 48 hours. Because patients on methadone maintenance are dosed every 24 hours, the period of even partial pain relief with this medication is small. Therefore, contrary to popular belief, clinicians cannot count on a patient’s once-daily methadone dose to treat pain. Additional therapies above and beyond the methadone are required. Anecdotally, some patients on methadone maintenance report obtaining 6 to 8 hours of analgesia from their usual maintenance methadone dose and thus may respond well to either an afternoon or evening dose of a long-acting opioid analgesic to control their pain over the course of the day.

For patients with opioid dependence that is being treated with buprenorphine maintenance therapy, use of concurrent opioid analgesics is complicated by buprenorphine’s pharmacodynamics: 1) a very high affinity for the opioid receptor, and 2) only partial opioid agonist activity at that receptor. Because of its high

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receptor affinity, buprenorphine displaces or competes with full opioid agonist analgesics when given concurrently or following administration of these medications. This may precipitate a severe opioid withdrawal syndrome.113 Buprenorphine itself provides analgesia,81 but with limitations. Because of buprenorphine’s partial agonist properties, the analgesia it provides reaches a ceiling that cannot be overcome with increasing doses, and the duration of analgesia is only 4 to 8 hours, substantially shorter than its 24 to 48 hours of opioid withdrawal suppression. Therefore, patients taking buprenorphine for opioid dependence treatment must discontinue this medication if treatment of their chronic pain requires full-agonist opioids. Prior to taking this step, physicians and patients together will need to weigh the risks and benefits: 1) the risks of prescription medication abuse and potential relapse to drug use without buprenorphine; and 2) the potential improvements in pain and function that might be gained from treatment with full-agonist opioids.

Patients in recovery also may have specific preferences about types of pain medications. They may recognize better than physicians their risk of relapse if given opioids and may not want these.104 In a study of 20 patients with a past history of substance abuse, 30% relapsed after being given ongoing opioids for pain.112 On the other hand, surveys of drug users demonstrate that untreated pain can be a trigger for relapse or continued use among patients with past or current substance use disorders.16,24 A prescription opioid agreement may help provide a measure of control that recovering addicts often fear losing when taking these and other medications.

**MONITORING FOR AND RESPONSE TO ABERRANT DRUG-TAKING BEHAVIOR**

Given the concerns of abuse and diversion of prescription opioids, monitoring for aberrant drug-taking behavior becomes an important part of chronic pain management among patients with substance use disorders.

Gourlay et al advocate taking a “universal precautions” approach to this.113 The authors argue that this approach lessens the mistrust between physicians and patients because it makes no assumptions about particular groups of patients, it puts no one on the defensive, and it is less likely to lead to undertreatment of pain. It may actually be a more effective way of identifying true prescription opiate abuse in that it puts in place the same safeguards for everyone.

A universal approach to monitoring for aberrant drug-taking behavior involves 5 components: 1) assessing response to therapy; 2) use of contracts and/or agreements; 3) urine toxicology testing; 4) pill counts; and 5) developing a differential diagnosis of observed aberrant drug-taking behaviors.

**ASSESSING RESPONSE TO THERAPY**

Therapeutic response to opioids can be assessed using the four “As”: Analgesia (pain relief), Activities of daily living (psychosocial functioning), Adverse effects, and Aberrant drug-taking behavior.114 Pain intensity and functional scales should be routinely used at baseline and at follow-up visits. If improvements are not apparent therapeutic changes should be made. Assessment for medication adverse effects and aberrant drug-taking behaviors should be monitored at each visit.

**USE OF CONTRACTS/AGREEMENTS**

Patients with chronic pain who are to receive prescription opioids should be willing to participate in a jointly developed agreement outlining the indications for the medications, risks of treatment, appropriate use of the drugs, methods of monitoring for prescription drug abuse, including urine toxicology testing and pill counts, and consequences of inappropriate behavior.104,113 Whereas little data exist on the efficacy of written agreements in decreasing aberrant medication-taking behavior, there is no evidence that their use is detrimental to treatment.115 Patients unwilling to do this may be at higher risk for aberrant drug-taking behavior.119 For patients with a past or current substance use disorder, the agreement may include the provision of limited amounts of opioids at one time with assessments and new prescriptions provided at frequent visits to the physician and/or nurse, possibly every day to once a week or every 2 weeks. To avoid patients having difficulties in filling these multiple prescriptions, physicians may need to coordinate such a schedule with a patient’s insurance agency. Multiple examples of opioid agreements are available.115,116

**URINE TOXICOLOGY TESTING**

Random urine toxicology testing is a way to confirm appropriate medication usage and detect illicit drug use.117 In methadone treatment programs, such tests are performed regularly according to federally mandated strict chains of custody that require observed urine specimen production.118 Primary care settings typically cannot go to these extremes, but for urine toxicology test results to have meaning for a patient’s treatment, samples should be tested for authenticity. Relatively easy measures to help authenticate samples is to employ temperature strips or temperature-sensitive urine specimen cups, checking urine creatinine levels to ensure that samples have not been diluted with tap water, and establishing a chain of custody procedure for how to handle urine samples that makes practical sense for each setting.117

Like any laboratory test, urine toxicology is not perfect. Several assays exist, and laboratories are not universal in which initial screening assay they use to
test for various drugs. Some of the less expensive assays cross-react with medications such as efavirenz or ranitidine, causing false-positive results.\textsuperscript{119,120} Therefore, it is crucial for clinicians to obtain detailed medication histories including all over-the-counter and herbal medications taken by the patient before sending urine for toxicology testing. It often also is helpful to become familiar with particular laboratories, understanding which assays they use, and what limitations these have. In addition to looking for drugs of abuse, toxicology tests can serve as a compliance measure in verifying that the patient is taking the prescribed medication.\textsuperscript{117}

Finally, not all substances of abuse will be found on routine screening tests. For example, most assays do not routinely screen for methadone. This requires a specific request to the laboratory.

**PILL COUNTS**

Patients should be expected to bring any remaining prescribed opioids to each clinic visit. Physicians can then enlist a nurse or other clinic staff in conducting pill counts. Pill counts can verify that the patient is taking the opioid analgesic as prescribed. Although this does not preclude patients from hoarding medications obtained from other sources at home, this practice may reveal inconsistencies in medication usage and sends a message to the patient of the physician’s involvement in their pain management. Pain care team members also can assist in calling patients in for random pill counts if a situation warrants further investigation and scrutiny.\textsuperscript{104}

**DIFFERENTIAL DIAGNOSIS OF ABERRANT DRUG-TAKING BEHAVIORS**

Aberrant drug-taking behavior can signify the development of prescription opiate abuse. However, other possible causes of these actions include unrelieved pain, psychiatric disorders, or criminal activity on the part of individuals whose only intention is to sell the medications.\textsuperscript{121}

In the case of unrelieved pain, aberrant drug-taking behaviors arise when a patient cannot obtain tolerable relief with a prescribed dose of analgesic, and seeks alternate sources or increased doses, a phenomenon called “pseudoaddiction.”\textsuperscript{122} On the other hand, patients receiving good pain relief may exhibit aberrant drug-taking behaviors because they fear not only the reemergence of pain but also the emergence of with-

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<td>Frequent unauthorized dose escalations after being told this is inappropriate</td>
<td>Unwilling to consider other medications or nonpharmacologic treatments</td>
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![Figure 1. Continuum of Aberrant Drug-Taking Behaviors](image-url)
drawal symptoms. Known as "therapeutic dependence," these behaviors are actually efforts to maintain a tolerable level of comfort.

**Predicting and Responding to Aberrant Drug-Taking Behavior**

Making the distinction between appropriate pain relief seeking and prescription opiate abuse or criminal intent can be extremely difficult because there is no universal agreement on how to interpret aberrant drug-taking behavior. Several researchers have attempted to identify predictors of aberrant drug-taking behaviors and prescription opiate abuse to guide risk stratification and monitoring of patients prior to the initiation of these medications.

In an observational study of chronic pain patients managed in a pain specialty center, Michna et al identified low- and high-risk groups for aberrant drug-taking behaviors based on family and personal substance use history and prior legal problems. In comparing the high-risk with the low-risk group, the authors found that a larger percentage of high-risk patients reported past mental health problems, multiple motor vehicle accidents, nicotine dependence, and had more lost or stolen prescriptions. Subsequently, these individuals had a significantly higher incidence of urine toxicology screens positive for illicit substances than did the low-risk patients. There were no significant differences between the 2 groups in the rate of unsanctioned dose escalations, unscheduled clinic or emergency department visits, multiple phone calls, or concern from significant others.

Using a sample of chronic pain patients seen in one pain clinic, Webster and Webster recently validated a self-administered Opioid Risk Tool (ORT) as a brief screening instrument to predict which chronic pain patients prescribed opioid analgesics develop aberrant behavior. The ORT measures risk factors including personal and family histories of substance abuse, age, history of sexual abuse, and presence of psychiatric conditions. Of the 185 men and women in the study, 55% had a personal history of substance abuse. The authors categorized the patients as being at high, moderate, and low risk for aberrant drug-taking behavior based on selected cut-off points from the ORT. After a year of treatment and observation, the researchers found that 94% of the low-risk group did not exhibit any aberrant drug-taking behaviors, 91% of those in the high-risk group displayed at least 1 aberrant behavior, but only 28% of those with moderate risk did so. The authors reported excellent discrimination of the ORT for both men and women, but recommended further validation across groups with different demographic characteristics before the tool could be applied universally.

Finally, Chabal et al, with the help of an expert committee, developed and tested a clinical checklist to define prescription opiate abuse among chronic pain patients seen in a pain clinic. Their results suggest that the presence of 3 or more aberrant drug-taking behaviors significantly predicted development of the signs of prescription opiate abuse (eg, legal problems, needing drug treatment, and dropping out of care) within a year. A history of substance abuse was not predictive of prescription opiate abuse in this study.

Although further work is needed to clearly define who is at the highest risk for prescription opiate abuse, a continuum of aberrant drug-taking behaviors (Figure 1) and a list of risk factors for prescription opiate abuse can be developed based on these and other studies (Table).127,128

Approaching a patient about aberrant drug-taking behavior is often uncomfortable, and can be confrontational. To minimize confrontation, the physician should use a nonjudgmental stance, and should ask...
open-ended questions with clear statements regarding concerns about observed warning signs (Figure 2). If it is suspected that the patient’s aberrant drug-taking behavior is caused by prescription opiate abuse or addiction, stopping the opioid analgesics may be appropriate. At that point, such patients will require substance abuse treatment, either through referral or office-based treatment with sublingual buprenorphine, which can appropriately address the newly diagnosed problem of prescription medication abuse. They also will require reassurance that they will not be abandoned, and that the physician will continue to manage their pain using nonopioid analgesics and nonpharmacologic treatments. Because of the physical dependence on opioids, the particular opioid analgesics should be tapered over weeks to prevent significant withdrawal symptoms.

CONCLUSION

Despite limitations in the literature, patients with underlying addictive disorders are at high risk for developing chronic pain, which adds a layer of complexity to already complicated patients. Because of limited access to pain and addiction medicine specialists, these patients often seek help from primary care physicians, who may feel overwhelmed with and uncertain about how to address these issues. Although more extensive, high-quality evidence is needed to help guide appropriate management of these comorbid conditions, primary care physicians still face the dilemma of how to treat the patient presenting with chronic pain and addiction. Undertreatment of pain, relapse to drug use, and dissatisfied patients and physicians result when there is no well thought through, systematic approach to caring for patients with chronic pain and past or current addiction.

Based on the current best evidence available and expert clinical guidelines, an approach to this group involves thoroughly assessing the severity of both the chronic pain and the addiction; appreciating that pain perception may differ in those with addictive disorders for genetic, psychologic, and biochemical reasons; combining pharmacologic and nonpharmacologic interventions that reduce pain and improve function; and using mutually agreed upon treatment agreements to ensure consistent, safe, and effective care. Finally, physicians should recognize and address their own attitudes, biases, limits of knowledge, and fears, which may impact the trust and rapport that is crucial to the successful pain management of patients with substance use disorders.

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