



Prescription opioid use disorder:

A complex clinical challenge

Understanding patients' aberrant medication-taking behaviors can greatly aid treatment

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You've been treating Mr. H, a 54-year-old factory worker and tobacco user, for depression that developed after a work-related back injury and subsequent disability. His depression has had a fair response to an antidepressant. He also has been maintained on chronic opioids (morphine and oxycodone/acetaminophen) for 18 months by his primary care physician (PCP). At the end of your appointment, he asks you for a refill of the opioids because he "ran out" early because of increased night pain and resultant insomnia and "stress." He clarifies he has asked for early refills before from his PCP, but lately he has been denied. Because you "seem to listen to me more," he asks for your help. How should you manage Mr. H?

Opioids are among the most commonly misused prescription drugs in the United States.¹ In 2008, poisoning was the leading cause of death from injury in the United States; roughly 90% of poisonings resulted from drug exposure, and >40% of these drug poisonings were from prescription opioids.² The Centers for Disease Control and Prevention estimates that the number of emergency department (ED) visits for nonmedical use of opioids increased 111% between 2004 and 2008, from 144,600 to 305,900 visits.³ The highest number of visits were for use of oxycodone, hydrocodone, and methadone.³

Increased prescribing of opioids and overdose deaths attributable to prescribed opioids have raised concern among physicians about how to effectively treat pain as well as prevent, recognize, and manage aberrant medication-taking behaviors (AMTBs). Psychiatrists are well-positioned to screen and manage their own patients for prescription opioid use disorder (POUD) or collaborate with opioid prescribers to accomplish the same.

continued



Prescription opioid use disorder

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Strategies to reduce prescription opioid misuse include drug testing, restricting early refills, and frequent office visits



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Table 1

Terminology related to prescription opioid use disorder

Term	Definition
Chronic pain ^a	Pain that extends beyond the expected period for healing (6 months), initiated by tissue damage, but perpetrated by the interaction of physiologic, affective, and environmental factors
Chronic nonmalignant pain ^a	Chronic pain associated with diverse diagnoses and syndromes that are not terminal but affect the patient's function
Appropriate use ^a	Taking a prescription as prescribed, and only for the condition indicated
Misuse ^a	Taking a prescription for a reason or at a dose or frequency other than for which it was prescribed; this may or may not reflect POUD
Drug-seeking behaviors	Patient behaviors directed toward obtaining controlled substances, driven not by amelioration of the condition for which the medication was indicated but rather by other maladaptive gains; this may or may not reflect POUD
Chemical coping	Taking a controlled substance medication to relieve psychological problems (eg, to relieve low mood, anxiety, insomnia) and for reasons other than the purpose for which it was prescribed; this may or may not reflect POUD
Aberrant medication-taking behaviors ^a	Taking a controlled substance medication in a manner that is not prescribed; causes for this may include: <ul style="list-style-type: none"> • lack of understanding about how to take the opioid appropriately • external pressures, such as to give to another person for his or her pain • chemical coping • pseudoaddiction (see below), including: <ul style="list-style-type: none"> – physical tolerance and resultant inadequate pain control – opioid-resistant pain – opioid-induced hyperalgesia – progression of their pain generator or disease • addiction or substance use disorder (such as POUD) • diversion
Pseudoaddiction	An iatrogenic syndrome of “addiction-like” behaviors in which the patient seeks opioids to relieve pain—such as seeking different doctors, self-adjusting the opioid dose, early refills of opioids, etc.—rather than to achieve pleasure or other nonpain-related effect. At times mistaken for true addiction, these behaviors tend to resolve and function improves once analgesia is better addressed

^aThese terms and definitions are adapted from reference 4. The remaining terms and definitions were developed by the authors

POUD: prescription opioid use disorder

Clarifying terminology

Terminology used to describe POUD and related conditions often is poorly defined or loosely applied. Because emotions often enter discussions between patients and physicians about problems related to opioid therapy, nonstigmatizing and more objective terminology is needed, and clinicians are working toward standardizing this. Relevant terms are defined in **Table 1**.⁴

The DSM-5 Substance Use Disorders Work Group has proposed using the term opioid use disorder (OUD) to replace the term opioid dependence.⁵ The hope is that removing the word “dependence” from the diagnostic term will reduce confusion between “dependence” due to expected physical de-

pendence (tolerance, withdrawal) on medically prescribed opioids vs true addiction (currently defined as “opioid dependence” in DSM-IV-TR). This Work Group also has proposed combining opioid abuse and opioid dependence criteria into a single diagnosis of OUD, and adding “craving” to the criteria. For the complete proposed criteria, see www.dsm5.org/ProposedRevisions/Pages/proposedrevision.aspx?rid=460. These changes are still under review. In this article, we use the term POUD.

POUD and chronic pain

The incidence of POUD during opioid therapy for pain is unknown.⁶ Some re-

searchers have suggested it may be as low as 0.2%,⁷ while others estimate that rates of POUD in patients with chronic pain may be similar to those in the general population: 3% to 16%.⁸ When applying the proposed DSM-5 criteria to patients receiving long-term opioid therapy for noncancer pain, the lifetime prevalence of POUD may be as high as 35%.⁹

Prescribers may be contributing to POUD. Roughly 76% of opioids used for nonmedical purposes were prescribed to someone else, 20% were prescribed to the user, and 4% came from other sources.¹ Strategies to reduce POUD risk may be underused. In a retrospective cohort study of 1,612 patient electronic medical records from 8 primary care clinics that managed patients with long-term opioids for chronic noncancer pain (average prescribing duration of 2 years duration, ≥ 3 monthly prescriptions in 6 months), researchers evaluated how often prescribers used 3 risk reduction practices:

- urine drug tests
- regular office visits (≥ 1 every 6 months and within 30 days of changing opioid treatment)
- restricted early refills (≤ 1 opioid refill more than a week early).¹⁰

Risk factors for opioid misuse included age < 45 , having a substance use disorder or other psychiatric disorder, and using tobacco. Only 8% of all patients received a urine drug test, only one-half had regular office visits, and 23% received > 1 early refill. Researchers found that even for high-risk patients, these strategies were used infrequently. Less than one-quarter of patients with ≥ 3 risk factors ever had a drug test, and those at increased risk were more likely to receive > 1 early refill but no more likely to have more frequent visits. Issues such as patient entitlement, lack of physician education, and time constraints may explain why these strategies are not used more often.¹¹

No one procedure or set of variables is sufficient to identify chronic pain patients who may be at risk for POUD. However, a history of drug or alcohol use disorders may be a significant risk factor.^{12,13}

Few tools have been developed to help identify those at risk of AMTBs or POUD, and all have limitations.^{4,14} Recommended

Table 2

Aberrant medication-taking behaviors and POUD risk

Behaviors more suggestive of POUD
Deterioration in function (work, social)
Illegal activities (selling medication, forging prescriptions, buying from non-medical sources)
Altering the route of administration (snorting, injecting)
Multiple episodes of 'lost' or 'stolen' prescriptions
Resistance to change therapy despite negative outcomes
Refusal to comply with toxicology testing
Concurrent, active abuse of alcohol, illegal drugs
Use of multiple physicians or pharmacies to obtain the prescription
Behaviors less suggestive of POUD
Complaints for more medication
Medication hoarding
Requesting specific pain medications
Openly acquiring similar medications from other providers
Occasional unsanctioned dose escalation
Nonadherence to other recommendations for pain therapy

POUD: prescription opioid use disorder
Source: Reference 17

self-report measures include the Current Opioid Misuse Measure and the Opioid Risk Tool.¹⁵ A review of studies in which these kinds of tools were developed revealed limited evidence for their use; most studies had methodological shortcomings, did not use standardized AMTB criteria, and provided little assessment of whether these tools changed clinician behaviors or improved patient outcomes.¹⁶

Evaluating AMTBs

Although diagnosing POUD in pain patients receiving chronic opioids can be challenging, assessing for AMTBs typically is helpful. Once AMTBs are identified, they can be examined to determine what drives their expression (*Table 1*⁴ and *Table 2*¹⁷). However, often it is easier to identify AMTBs than to

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Patients with a history of drug or alcohol abuse may have a higher risk of prescription opioid use disorder



Prescription opioid use disorder

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Interpret aberrant medication-taking behaviors cautiously because no single behavior alone is indicative of POUD

See this article at CurrentPsychiatry.com for a box that describes steps the FDA has taken to prevent POUD

Table 3

Identifying addiction in pain patients: Limitations of DSM-IV-TR

DSM-IV-TR substance dependence criteria

Challenges in using criterion to diagnose prescription opioid use disorder

Tolerance	Expected with prolonged opioid compliance
Physical dependence, withdrawal	Expected with prolonged opioid compliance
Use of larger amounts or longer than initially intended	Emergence of pain may demand increased dose or prolonged use
Multiple failed attempts to cut down or control	Emergence of pain may deter dose reduction or cessation
Time spent finding, using, or recovering	Difficulty finding adequate pain treatment may increase time spent pursuing analgesics. However, time spent recovering from overuse may suggest addiction
Given up or reduced important activities	Valid criteria—engaging in activities is expected to increase, not decline, with effective pain treatment
Continued use despite knowledge of negative consequences	Valid criteria—no harm is anticipated from analgesic opioid use for pain (see Table 4)

Source: Adapted from reference 6

interpret their origins; as much as 30% to 50% of patients who complain of chronic pain may have primary substance dependence to sedatives, opioids, or both.¹¹

Although AMTBs are common among chronic nonmalignant pain patients,^{18,19} how often AMTBs reflect underlying POUD is uncertain.⁷ It is critical to interpret AMTBs with a balance of caution and care: “react therapeutically, not punitively.”²⁰ Categorizing a patient’s AMTB as more or less likely to support a POUD diagnosis can be helpful, but is not conclusive (**Table 2, page 17**).¹⁷ Clinical correlation often is required. No single AMTB alone is indicative of POUD. When evaluating AMTBs, the treating provider should use a nonjudgmental stance, and consider obtaining collateral data from people who can provide differing perspectives of the patient’s behaviors, such as other clinicians, significant others, family, etc. (a release of information from the patient may be required). Another source of collateral data is prescription monitoring databases. These databases typically are state-based and provide electronic access to prescription information, allowing you to search for patterns—ie, use of multiple prescribers or pharmacies, undisclosed prescriptions, etc. Interest in establishing a single, federal database has been increasing, but striking a balance between carefully moni-

toring for AMTBs and protecting privacy remains unresolved.

DSM-IV-TR diagnostic criteria for opioid dependence²¹ can be challenging to interpret in patients who are prescribed opioids for pain (**Table 3**).⁶ To clarify interpretation, the Liaison Committee on Pain and Addiction of the American Society of Addiction Medicine (ASAM) has provided an outline of possible indicators of addiction in pain patients (**Table 4**).⁶ This was a consensus statement from the American Pain Society, the American Academy of Pain Medicine, and ASAM.

Assessment is primarily clinical and requires an awareness of appropriate terminology, an index of clinical suspicion, and expertise teasing apart pain, addiction, and pseudoaddiction. In our experience, it is helpful to ask a chronic pain patient whom you suspect might have POUD, “Have you ever used your prescribed opioids for reasons other than improving function or reducing pain, such as for getting a ‘high,’ managing stress, escaping from problems, etc.?” An affirmative response suggests an underlying problem with use of prescribed opioids, indicating a need for more careful questioning to determine if AMTBs or POUD coexist with chronic pain.

Drug testing can help determine if a patient is taking opioids that are not prescribed—as well as illicit drugs or alco-

Table 4

Possible indicators of addiction in pain patients

ASAM-APS-AAPM behavioral criteria

Examples of specific behaviors in opioid therapy for pain

Impaired control over opioid use	Patient requests early refills, frequently reports loss or theft of medication. Withdrawal noted at follow-up appointments despite having an adequate quantity of medication prescribed
Continued use despite harm from opioids	Patient exhibits declining function, opioid intoxication, persistent oversedation from opioids
Preoccupation with opioids	Patient ignores non-opioid interventions for pain, makes recurrent requests for opioid dose escalation (or complains of increasing pain) despite absence of disease progression or despite opioid dose increase by provider

AAPM: American Academy of Pain Medicine; APS: American Pain Society; ASAM: American Society of Addiction Medicine

Source: Adapted from reference 6

hol—and confirm the presence of those that are prescribed. Toxicology screening should include opioids typically screened for (eg, morphine, codeine, heroin) and those for which additional tests may be required (eg, semi-synthetics such as oxycodone and hydrocodone and synthetics such as fentanyl).

Helping POUD patients

Goals of treatment include establishing a therapeutic alliance, educating patients about POUD, reducing relapse risk, and optimizing overall health (including pain and physical function). The ASAM Patient Placement Criteria²² provide guidance regarding level-of-care decisions. Treatment ideally includes a combination of education about POUD and its relationship to chronic pain, pharmacotherapy, psychotherapy—such as motivational enhancement therapy, 12-step facilitation therapy, cognitive-behavioral therapy, and relapse prevention—and referral to self-help groups such as Narcotics Anonymous or Pills Anonymous. Importantly, if pain is genuine, it requires treatment.

Pharmacotherapy. Methadone is recommended as the standard of care for OUD by the National Institutes of Health. Methadone is a full opioid agonist that decreases illicit opioid use, mortality, and related problems and requires highly structured treatment approaches under federal and state regulation. POUD patients may have higher rates of

methadone maintenance treatment retention than heroin-dependent patients.²³ Published trials of buprenorphine for OUD have shown good treatment retention and reduction in illicit drug use and adverse events.²⁴ Buprenorphine also decreases mortality among OUD patients.

The first large-scale, randomized clinical trial of buprenorphine specifically for POUD included 653 treatment-seeking outpatients.²⁵ This study was designed to approximate clinical practice and included buprenorphine/naloxone, recommended abstinence, and self-help; one-half of participants received intensive addiction counseling. POUD patients were most likely to reduce prescription opioid misuse during buprenorphine/naloxone treatment. If tapered off buprenorphine/naloxone, even after 12 weeks of treatment, the likelihood of an unsuccessful outcome was high. Moreover, opioid dependence counseling did not seem to afford any difference in outcomes. However, despite clinical effectiveness, over the last decade only 19% of patients admitted primarily for OUD treatment (other than heroin) were planned to be offered buprenorphine or methadone.²⁶

A Cochrane review of oral naltrexone for OUD found that the drug was no better than placebo but concluded that available evidence does not allow an adequate evaluation.²⁷ Opioid antagonists may be of value to patients who do not want to take agonists or partial agonists. Extended-release naltrexone also is available to treat OUD.

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Treatments for patients with POUD include education, pharmacotherapy, psychotherapy, and referral to self-help groups

See this article at
CurrentPsychiatry.com
for a list of precautions
to take when prescribing
opioids long-term

continued



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For a **Box** that details steps the FDA and others have taken to prevent POUD and a **Table** that outlines precautions to incorporate when prescribing opioids long-term, see this article at CurrentPsychiatry.com.

CASE CONTINUED

A closer evaluation

After expressing your appreciation for Mr. H's kind words and empathy for his chronic pain, you redirect him to his PCP. You ask him to sign a release of information so you and his other clinicians can coordinate his care. When discussing Mr. H with his PCP, you learn the patient has made limited requests for early refills and dose escalation primarily in relation to inadequate pain control and function, has genuine pain pathology, and is greatly distressed over his inability to work. No other AMTBs are present, and a check of the state prescribing database reveals that Mr. H did receive a small quantity of opioids from an ED on 1 occasion.

You and Mr. H's PCP agree this is "pseudo-addiction" but want to watch Mr. H more closely and look for ways to coordinate his care. The PCP agrees to implement a prescribing agreement, start drug testing (including for the prescribed opioids), and reassess maximizing Mr. H's function and pain management while you address his combined pain, depression, insomnia, and tobacco use.

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Related Resources

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Drug Brand Names

Buprenorphine • Subutex	Methadone • Dolophine,
Buprenorphine/ naloxone • Suboxone	Methadose
Codeine • Tylenol with codeine, others	Morphine • Roxanol
Fentanyl • Duragesic, Actiq	Naltrexone extended- release • Vivitrol
Hydrocodone • Lortab, Vicodin, others	Oxycodone • OxyContin, Roxicodone

Disclosures

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Bottom Line

Understanding the terminology related to prescription opioid use disorder (POUD) and causes for aberrant medication-taking behaviors (AMTBs) can greatly assist treatment. No single AMTB alone indicates POUD; assessment primarily is clinical. Educating patients about POUD can reduce relapse risk and improve overall health.

Taking steps to prevent prescription opioid use disorder

The FDA has moved toward a risk evaluation and mitigation strategy (REMS) for opioids prescribed for pain that requires clinicians to receive training and certification in prescribing opioids for pain as well as identifying and reducing the risk for prescription opioid use disorder (POUD).^a In 2011, the Obama administration developed an action plan to better address prescription drug abuse that required several federal agencies to develop programs and policies to address this growing problem; this plan was updated for 2012 (the complete National Drug Control Strategy 2012 is available at www.whitehouse.gov/sites/default/files/ondcp/2012_ndcs.pdf). The American Society of Addiction Medicine

has issued a public policy statement that supports the federal approach and outlines other means to reduce POUD.^b

Some pain specialists recommend requiring patients to sign an Opioid Pain Management Agreement that includes an “exit strategy” before the first opioid prescription is written. These agreements incorporate elements of “universal precautions” to take when prescribing opioids long term.^{c,d} Although not well-studied, prescribing agreements may help educate patients and providers on how to interact in the management of pain with opioids in a way that is objective and empathic, and may reduce POUD risk.

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Table

Universal precautions with chronic opioid management

Goals of therapy: partial pain relief and improvement in physical, emotional, and/or social functioning
Requirement for a single prescribing provider or treatment team
Limitation on dose and number of prescribed medications
Prohibition of changing dosage without discussion with the provider first
Monitoring patient adherence; discuss the use of ‘pill counts’
Prohibition of use with alcohol, other sedating medications, or illegal drugs without discussion with the provider
Agreement not to drive or operate heavy machinery until abatement of medication-related drowsiness
Responsibility to keep medication safe and secure
Prohibition of selling, lending, sharing, or giving medication to others
Limitations on refills—only by appointment, in person, and no extra refills for running out early
Compliance with all components of overall treatment plan (including consultations and referrals)
Biological testing to screen for drugs of abuse or alcohol as well as to confirm the presence of prescribed opioids
Adverse effects and safety issues, such as the risk of physical dependence and addiction behaviors
The option of sharing information with family members and other providers, as necessary, with the patient’s consent
Need for periodic reevaluation of treatment
Reasons for stopping opioid therapy
Consequences of nonadherence with the treatment agreement
Source: Gourlay DL, Heit HA, Almahrezi A. Universal precautions in pain medicine: a rational approach to the treatment of chronic pain. <i>Pain Med.</i> 2005;6(2):107-112.