Consensus-Based Treatment Approaches for Managing Concerning Behaviors in Patients on Long-term Opioid Therapy for Chronic Pain: Case-Based Applications

William C. Becker, MD; E. Jennifer Edelman, MD, MHS; Joanna L. Starrels, MD, MS; Soraya Azari, MD; Payel Roy, MD; Sarah R. Young, PhD, LMSW; Jane Liebschutz, MD; and Jessica S. Merlin, MD, PhD

Abstract

Guidelines recommend careful monitoring of patients on long-term opioid therapy for chronic pain to assess for concerning medication-taking behaviors that may signal opioid misuse or the presence of a substance use disorder. However, specific management strategies to guide providers if concerning medication-taking behaviors emerge are lacking. Therefore, we recruited a Delphi panel—42 experts in chronic pain and opioid prescribing—to develop consensus-based treatment approaches to guide management of the 6 most common and concerning behaviors identified: missing prescriber appointments, taking opioids for symptoms other than pain, using more opioid medication than prescribed, asking for an increase in opioid dose, aggressive behavior, and alcohol and other substance use. The results of that process are published as a separate study. The purpose of the present study was to present clinical cases in which concerning medication-taking behaviors arise in the course of long-term opioid therapy and demonstrate for readers how the Delphi panel’s consensus-based approaches could be applied.

Because of increased awareness of opioid-related harms and concerns about lack of benefit, guidelines promote frequent monitoring of individuals on long-term opioid therapy (LTOT) for chronic pain. One of the main purposes of this monitoring, alongside assessing effectiveness and harms, is to identify concerning medication-taking behaviors that may indicate misuse or signal the presence of an underlying substance use disorder. In terms of how prescribers should respond to these behaviors, the CDC Guideline for Prescribing Opioids for Chronic Pain discusses broad approaches, for example, tapering when benefits do not outweigh harms, but does not address specific management strategies because of lack of evidence. Noting this gap in the literature, we recruited a Delphi panel—42 experts in chronic pain and opioid prescribing—to develop consensus-based treatment approaches to guide management of the 6 most common and concerning behaviors identified: missing prescriber appointments, taking opioids for symptoms other than pain, using more opioid medication than prescribed, asking for an increase in opioid dose, aggressive behavior, and alcohol and other substance use. The results of that process are published as a separate study.

Although future studies testing efficacy and implementation of the consensus-based treatment approaches as care algorithms/protocols are planned, we recognize that providers in the field may be interested in learning more about how these treatment approaches might apply to patient care. Therefore, the purpose of this article was to guide practicing clinicians on application of the consensus-based treatment approaches in 3 cases in which concerning behaviors arise in the course of LTOT. To clarify some of the treatment approaches, we have selected illustrative qualitative text from Delphi panelists. This is not intended to be a
comprehensive clinical discussion of each case and detailed discussion of some practices aimed at mitigating opioid-related risk is beyond the scope of this article, for example, screening for unhealthy alcohol use, counseling on safe storage of medication, and prescribing naloxone. Also, although the Delphi study focused on concerning behaviors, it is important to note that potential adverse effects from LTOT are myriad (e.g., hyperalgesia, hypogonadism, and depression) and should also be factored into benefit-harm determinations.

Because the consensus-based treatment approaches were generated by a diverse group of generalists and specialists, we intend the discussion of each case to be relevant to generalists and specialists alike: any clinician who prescribes and manages outpatient opioid therapy for adults with chronic pain other than in hospice settings. We selected cases that in our experience are common in generalist and specialist practice: using more opioid medication than prescribed, missing prescriber appointments, and cocaine use. Of note, in each case, patients were properly counseled at treatment outset about the potential risks and benefits of LTOT as well as expectations of both the patient and the provider with regard to the treatment plan, including the need to offer (on the provider’s part) and engage in (on the patient’s part) a multimodal pain care strategy that included nonopioid and nonpharmacologic treatment modalities.

**CASE 1 PRESENTATION: USING MORE OPIOID MEDICATION THAN PRESCRIBED**

The patient is a 60-year-old man with mild chronic obstructive pulmonary disease, hypertension, and degenerative joint disease of the lumbar spine treated for many years with LTOT. He transferred pain care to his current primary care provider (PCP) 4 months ago from a pain management specialist. The PCP performed an initial comprehensive assessment and confirmed the patient’s current opioid dose from medical records, and continued the same therapy (morphine sustained release 30 mg twice daily with oxycodone immediate release [IR] 5 mg every 8 hours). After determining that benefits of LTOT were outweighing harms, the PCP discussed and signed an opioid treatment agreement with the patient. Five months later, the patient called 23 days into a 28-day prescription saying he was going to be “3 days short.” The patient reports tripping coming down the stairs and twisting his ankle on the stair landing; because of the resulting acute pain, he increased his morphine sustained release to 3 times daily and took some extra oxycodone.

**Applying Consensus-Based Treatment Approaches**

This episode falls into the category of using more opioid medication than prescribed. The patient’s independent decision to increase his dose contradicts the opioid treatment agreement and puts him at increased risk of overdose. According to the Delphi study, consensus-based approaches at this point include reviewing the opioid treatment agreement with the patient; ordering urine drug tests that day and more frequently; providing prescriptions at shorter intervals; discussing or referring for nonopioid therapies; discussing or assessing for a substance use disorder; individualizing the response to the patient’s behavior; and determining whether a pattern of behavior has been present (see Table 1). Each of these steps is discussed in detail below. Stopping opioid therapy immediately the first time such a behavior was observed was not endorsed by the expert panel.

**Continuation of the Case**

Consistent with the consensus-based treatment approaches, the PCP asked that the patient be scheduled for an urgent visit to assess and discuss the situation. A urine drug test was ordered. The PCP assessed the ankle pain and diagnosed a sprain without fracture. The PCP discussed with the patient that patient-initiated dose escalation is dangerous and against the guidance outlined in the opioid treatment agreement. She referred the patient for physical therapy and recommended ice, elevation, and nonsteroidal anti-inflammatory drugs. She probed further about other episodes of taking more medication than prescribed, which the patient denied, and queried the prescription monitoring program database, which revealed no additional prescriptions. After the patient left, the urine drug test returned positive for oxycodone (a semisynthetic opioid) but not opiates (consistent with the patient’s report of having run out of morphine 3 days earlier). The PCP’s overall assessment was that a pattern was not currently present but that closer monitoring
was warranted given the concerning behavior. The PCP prescribed a 2-week supply of medication at this visit—3 days early—and communicated that the patient would need to pick up prescriptions at 2-week intervals for a few months and demonstrate the ability to take the medications as prescribed for the therapy to be continued.

At the next 2 prescription pick-ups (2 weeks apart), urine drug test results were consistent with the prescribed therapy. However, on the third prescription pick-up, the urine drug test was positive for oxycodone but negative for opiates. Now concerned about a pattern of running out early, the PCP called the patient to discuss the findings. The patient admitted that he had run out early, despite his desire to cut back on the amount he was taking, and also acknowledged that between doses, he had a preoccupation with needing to take more medication. This prompted the PCP to consider the diagnosis of opioid use disorder (OUD) using the 11 Diagnostic and Statistical Manual of Mental Diseases (Fifth Edition) (DSM-5) criteria listed in the Supplemental Appendix, available online at http://mcpiqojournal.org/. It is important to note that the DSM-5 stipulates that 2 criteria, tolerance and withdrawal symptoms, do not contribute to a diagnosis of OUD among patients who are prescribed opioids for pain because these are common phenomena for long-term use of opioids even when taken as directed; on the other hand, the International Classification of Diseases, 10th Revision does include tolerance and withdrawal as criteria in “opioid dependence.” However, on further questioning by his PCP, this patient endorsed 2 other criteria—unsuccessful attempts to cut down and craving—that meet the 2-criteria threshold for mild OUD. Having made this diagnosis, the PCP discussed her concerns with the patient and then placed a referral to a specialist with buprenorphine certification for consideration of ongoing treatment for OUD. The patient agreed to accept the referral, so the PCP kept the opioids at the same dose until the appointment with the buprenorphine-prescribing specialist.

**Summary/Key Points**

In this case of using more opioid pain medication than prescribed, the consensus-based treatment approaches guided the PCP to recognize the concerning behavior, discuss it with the patient, make an assessment of whether a pattern was occurring, and increase frequency of monitoring. Importantly, immediate discontinuation was not endorsed by the Delphi panel. During the increased

---

**TABLE 1. Consensus-Based Treatment Approaches When Patients Use More Opioid Medication Than Prescribed**

| Patient behavior                                      | Treatment approaches                                                                 |
|-------------------------------------------------------|--------------------------------------------------------------------------------------|
| If first episode of using more opioid medication than prescribed | - Review opioid treatment agreement with the patient  
- Order urine toxicology tests that day and more frequently  
- Provide prescriptions at shorter intervals (eg, 2 weeks’ supply)  
- Discuss or refer for non opioid therapies (non opioid pharmacologic therapies, non pharmacologic therapies)  
- Determine if a pattern of behavior has been present  
- Discuss or assess for a substance use disorder  
- Individualize response to the patient’s behavior |
| If pattern confirmed without diagnosis of opioid use disorder | - Deny early refill, even on first ask |
| If incident diagnosis of opioid use disorder          | - Utilize pill counts  
- Make a referral to addiction treatment or related services  
- Make a referral to a pain specialist  
- Taper opioids |
monitoring period, a pattern emerged that was concerning for OUD and indeed this diagnosis was made. Whether treatment for OUD occurs “in house” or required referral to a specialist, one Delphi panelist commented that “an evaluation and subsequent treatment of OUD is invaluable in providing safe and effective care for [patients with OUD].” Although not covered in the case, a wide variety of nonopioid pharmacologic and nonpharmacologic treatments to address the patient’s chronic pain would be indicated before and after the diagnosis of OUD.

CASE 2 PRESENTATION: MISSING PRESCRIBER APPOINTMENTS

A 44-year-old woman with a medical history significant for obesity presents for chronic abdominal pain that began 5 years ago, just after bariatric surgery. She underwent extensive evaluation of the pain, including imaging and functional tests, by the bariatric surgeon and a pain specialist and they each concluded that the pain’s etiology was not amenable to intervention. The patient tried various nonpharmacologic treatments, such as dietary changes and stress reduction, and nonopioid analgesics, including acetaminophen and ibuprofen, with no effect. As a result, the surgeon initiated opioid pain medication several years earlier and eventually referred the patient back to primary care for pain management. At the time of transfer, she was prescribed oxycodone controlled-release (CR) 20 mg twice daily and oxycodone IR 5 mg 4 times daily as needed for severe pain. She reported moderate pain relief but ongoing interference with function and enjoyment of life due to pain. She had no personal or family history of substance misuse or mental illness.

The PCP reviewed the opioid treatment agreement with the patient and checked a urine drug test, which was appropriately negative for illicit substances and positive for oxycodone. In addition to continuing the current opioid regimen with monthly refills, the PCP referred the patient to a psychologist to help with pain self-management and a gastroenterologist with expertise in functional gastrointestinal disorders.

The patient was scheduled back with the PCP in 2 months with a nurse check-in at 28 days to pick up prescriptions without seeing the PCP. The patient missed the PCP appointment but called in to have medication ordered; she rescheduled at that time for the following month. In reviewing her chart at the rescheduled appointment, the PCP noted that she had also missed visits with the psychologist and the gastroenterologist. The patient reported that it was difficult in general for her to make appointments because she cannot afford to take time off from work because she supports 5 children. She stated that she did not realize that attending appointments was part of the opioid treatment agreement, which was reviewed with her again. She wanted to continue opioid therapy because she stated it helped her pain and overall function (eg, allowed her to work) but subsequently missed her next 2-month appointment with the PCP.

Applying Consensus-Based Treatment Approaches

This episode falls into the category of missing prescriber appointments, which interferes with the ability to monitor patients on LTOT and is inconsistent with a comprehensive pain treatment plan. In the case of missing appointments, the Delphi panel reached consensus that the prescriber should determine whether a pattern of behavior has been present by talking to the patient or reviewing records; review the opioid treatment agreement with the patient; require appointment attendance if opioids are to be continued; and give the patient at least one chance to change behavior (see Table 2). The Delphi panel did not endorse stopping opioid therapy immediately at this point. Even though the patient has missed appointments, the opioids were benefitting the patient in terms of improved function. In addition, stopping immediately may precipitate withdrawal symptoms.

Continuation of the Case

The PCP’s office held her next prescription until her rescheduled appointment with the provider later in the week. At that time, there was a frank discussion of the need to maintain the treatment plan outlined in the opioid treatment agreement. The patient agreed to this plan and she and the PCP brainstormed ways in which to make it feasible for her to attend her appointments. She was told that if she does not keep her appointments, the opioids would be tapered. Her urine toxicology
test result was consistent with therapy. She subsequently missed her next PCP appointment and still had not attended a specialist visit.

**Applying Consensus-Based Treatment Approaches**

At this point, the patient has continued to miss appointments with the PCP and specialists, despite discussing this behavior and setting clear expectations with the PCP. According to the consensus-based treatment approach, tapering opioids is now endorsed, and the PCP could consider stopping opioid therapy immediately. As one participant mentioned, in agreement with tapering, “We require MD face-to-face visits every 90 days.”

**Continuation of the Case**

The PCP began a taper by lowering the dose of oxycodone CR to 10 mg twice daily and maintaining oxycodone IR at the current dose. Nonopioid pain treatments were discussed, but the patient declined to pursue them. The patient returned to the PCP’s office for her next scheduled appointment and was upset that her dose had been decreased but wanted to continue therapy. She and the PCP had another discussion about risks and benefits of opioids and devised a method for aligning her prescription pick-up with her physician appointments. She returned to see the PCP every month for the next 3 months. Her urine toxicology results were as expected and she remained stable on a lower dose of opioids, including some improvement in her abdominal pain, suggesting there may have been a component of opioid-induced gastrointestinal hyperalgesia on the higher dose. Evidence of improvement with dose lowering can be used by providers to help motivate patients to consider further dose lowering.

**Summary/Key Points**

Missing appointments with members of the care team, including PCPs, specialists, and ancillary staff, inhibits provider ability to provide a comprehensive approach to pain management and prevents appropriate monitoring of patients for benefits and adverse effects of therapy. Although missing appointments may not be indicative of heightened addiction risk, it is still concerning behavior in that the patient cannot be monitored by the provider at a safe interval. According to the Delphi participants, these behaviors should be addressed by reviewing the patient’s records, reviewing the opioid treatment agreement, requiring future attendance, and giving the patient at least one chance to change behavior.

**CASE 3 PRESENTATION: COCAINE USE**

The patient is a 50-year-old former marathon runner with severe osteoarthritis of the right knee and major depression. She had been followed up regularly by her PCP for about 6 months after transferring care from another provider in the same practice. Over the previous 5 years, she had tried multiple pharmacologic, nonpharmacologic, and interventional approaches to treat knee pain. At that time, she was taking oxycodone CR 20 mg twice per day, which decreased pain intensity and helped her to work part-time in retail. She had denied drug or alcohol use except for occasional drinks, and her urine drug test results had been consistent with her prescribed oxycodone. Six months into care with her PCP, a urine drug test unexpectedly returned positive for cocaine.

**Applying Consensus-Based Treatment Approaches**

With respect to use of illicit or nonprescribed substances, the Delphi panel endorsed
determining whether a pattern of behavior is present and discussing or assessing for a substance use disorder (see Table 3). They also endorsed reviewing the opioid treatment agreement with the patient and monitoring more closely with urine drug tests. The PCP had an appointment to see the patient again in 3 weeks.

To determine whether a pattern was present, all urine drug testing data available in the electronic medical record were reviewed. There was one previous test positive for cocaine 2 years before, but the previous provider had ordered drug tests only twice in the 2 years. A text search for “cocaine” in the electronic medical record found no mention of this episode, including in the previous provider’s notes at the time of the positive test result. The new provider called the patient to tell her that the urine drug test was positive for cocaine. She sighed and acknowledged that she used cocaine intranasally one time at a party several days before her last appointment. The provider thanked her for her honesty and asked how often she uses cocaine. She said it had been many years since she last used it, and she could easily avoid using it in the future, adding, “I’m not addicted, don’t worry.” The PCP reminded her about the risks of using drugs with opioids and that some drug-drug combinations can be lethal.

Her visit a month later included a thorough assessment for a substance use disorder (either cocaine or opioid), reviewing the 11 DSM-5 criteria. She did not meet criteria. The PCP reviewed the opioid treatment agreement with the patient, which included the expectation that the patient would avoid illicit drug use, and reiterated that if she continued to use other drugs, the risks of continued opioid therapy would be likely to exceed its benefit and may need to be discontinued (for suggested language in this conversation, see Supplemental Table, available online at http://mcpiqojournal.org/). She verbalized understanding and agreed to the plan. Considering the consensus-based treatment approaches, the next key question concerned whether there was a pattern of behavior present, as opposed to an isolated event. At this point, there was a potential pattern, in that she had a previous positive urine drug test result among the few tests performed 2 years ago. However, she reported rare use and available data do not contradict that. Therefore, the provider concluded that at that time there was no clear pattern of cocaine use or substance use disorder.

Without a clear pattern of use or a substance use disorder, one could consider tapering or stopping opioids; however, the PCP in this case decided not to because the benefits of opioids to the patient—specifically, helping maintain her work schedule—exceeded the risks at that time. If a pattern of cocaine use emerged in future visits, or any heroin use were to be identified, then Delphi panelists would endorse tapering or discontinuing opioids. On the basis of this approach, the provider developed a plan to see the patient every month to conduct routine monitoring, reassess substance use, and check a urine drug test.

**Continuation of the Case**

During the subsequent 6 months, urine drug tests returned negative for cocaine and positive for oxycodone. At that point, it was reasonable to continue routine monitoring at appropriate intervals (eg, urine drug tests and follow-up visits every 1-3 months). She continued to remain engaged in other aspects of her primary

| **TABLE 3. Consensus-Based Treatment Approaches When Patients Use Cocaine** |
|-----------------------------------------------|
| **Patient behavior** | **Treatment approaches** |
| First episode cocaine use | • Determine if a pattern of behavior has been present (eg, by talking to the patient or reviewing records) |
| | • Discuss or assess for a substance use disorder |
| | • Refer for addiction treatment or related services |
| | • Review opioid treatment agreement with the patient |
| | • Order urine toxicology tests more frequently |
| Pattern of cocaine use is uncovered or emerges after initial prescriber actions are instituted | • Taper opioids |
care and chronic pain treatment, including physical therapy and counseling visits.

Summary/Key Points
Illicit drug use is a common and concerning behavior among patients prescribed opioids. Most troubling is the use of other opioids such as heroin, or other central nervous system depressants such as alcohol or benzodiazepines, because of the risk of overdose. However, cocaine use was clearly also concerning to panelists. One Delphi panelist commented, “Even isolated cocaine use is worrisome.” The panel endorsed tapering opioids when a pattern of cocaine use is identified. However, in this case, the patient appeared to use cocaine very sporadically and continued to be engaged in other aspects of her care. As one expert from our Delphi panel suggested, the provider should assess “can the patient stop using cocaine? [and] are they getting benefit from the opioids?” In this case, the provider opted to continue the patient’s opioids, because the benefits of opioids outweighed their risks and cocaine use did not become a pattern. When asked to advise how to taper in such a similar situation, experts indicated that the rate of tapering would depend on the risks, for example, “If I am working with a patient who is mixing their opioids with cocaine [ie, taking simultaneously] …and are at great risk, we do it [taper] faster.”

CONCLUSION
These cases highlight 3 of the common and concerning behaviors among patients on LTOT—taking more medication than prescribed, missing prescriber appointments, and using cocaine—and demonstrate for readers the application of consensus-based treatment approaches designed to provide clinicians detailed guidance on the management of these behaviors. A common theme across case presentations is that abrupt cessation of opioids for incident concerning behaviors was not a consensus-based approach. Rather, reconnecting with the patient, reassessing the situation, and reviewing the treatment agreement coupled with more frequent monitoring were the consensus-based steps followed in these cases. We note that the cases were presented assuming clear, patient-centered communication regarding goals, risks, and potential benefits at the outset and portrayed providers behaving with equanimity and thoughtfulness throughout the evolution of each case. In reality, providers may behave quite differently from this and patients may bear the accumulated scars of fraught interactions with sometimes mistrustful or disengaged providers. In recognition of this, we recommend allowing patients some room to express frustration about previous interactions and if not explicitly saying so, showing patients by actions and words that your approach will be defined by empathy, respect, and a high regard for the patient’s safety, health, and well-being.

The findings generated by a Delphi panel of expert clinicians represent a consensus on best practices from a diverse group. We hope that case examples that illustrate application of the consensus-based treatment approaches may increase clinicians’ comfort and confidence managing behaviors in the course of LTOT that can be challenging and distressing to many clinicians.6,7 One limitation of these findings is that they do not address how to proceed when multiple kinds of concerning behaviors happen at the same time or in relatively quick succession, which may happen in clinical care. Our experience suggests that more kinds of concerning behaviors should elicit greater attention and intensified monitoring on the prescriber’s part but that patients should still have an opportunity to change the behaviors before discontinuation of LTOT. Also, adjudicating the presence of patterns of behavior is inherently a subjective determination that is at risk of being applied differentially across patients. As with all clinical decision making, we recommend that providers try to be aware of biases and establish practice norms that lessen risk of treatment variability. Another limitation is that the consensus-based approaches have not been tested in clinical trials. However, some of the steps—for example, transparent communication with patients and trying to identify patterns of behavior in order to adapt one’s assessment of an evolving condition—have inherent value in clinical care and are generally recommended in the management of chronic conditions. Future empirical testing of the efficacy and optimal implementation of the approaches may elucidate and enhance their utility for guiding clinical care for patients on LTOT for chronic pain. As guideline-concordant care moves away from LTOT as
a first-line treatment option, approaches for avoiding LTOT in the first place are also needed. In addition, although these case examples are meant to help clinicians faced with similar situations, we must emphasize that they should not replace the clinician’s individual judgment.

SUPPLEMENTAL ONLINE MATERIAL
Supplemental material can be found online at http://mcpiqojournal.org/. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: CR = controlled release; DSM-5 = Diagnostic and Statistical Manual of Mental Diseases (Fifth Edition); IR = immediate release; LTOT = long-term opioid therapy; OUD = opioid use disorder; PCP = primary care provider

Grant Support: This work was supported by grant K23MH104073-01A1 (Principal investigator: Jessica S. Merlin, MD, PhD) from the National Institutes of Health. Study sponsors had no role in study design; in the collection, analysis, and interpretation of data; in the writing of the manuscript; or in the decision to submit the manuscript for publication.

Potential Competing Interests: Dr. Merlin reports research funding from the opioid postmarketing requirement consortium for a Food and Drug Administration-mandated observational study about the risks of extended-release/long-acting opioids. The rest of the authors report no competing interests.

Correspondence: Address to William C. Becker, MD, VA Connecticut Healthcare System, Mail Stop 151B, 950 Campbell Ave, West Haven, CT 06516 (william.becker@yale.edu).

REFERENCES
1. Chou R, Turner JA, Devine EB, et al. The effectiveness and risks of long-term opioid therapy for chronic pain: a systematic review for a National Institutes of Health Pathways to Prevention Workshop. Ann Intern Med. 2015;162(4):276-286.
2. Dowell D, Haegerich TN, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain – United States, 2016. MMWR Recomm Rep. 2016;65(1):1-49.
3. The Opioid Therapy for Chronic Pain Work Group. VA/DoD clinical practice guideline for opioid therapy for chronic pain. 2017. http://www.healthquality.va.gov/guidelines/Pain/cot/. Accessed October 31, 2017.
4. Merlin JS, Young SR, Azari S, et al. Management of problematic behaviors among individuals on long-term opioid therapy: protocol for a Delphi study. BMJ Open. 2016;6(5):e011619.
5. Merlin JS, Young SR, Starrels JL, et al. Managing concerning behaviors in patients prescribed opioids for chronic pain: a Delphi study. J Gen Intern Med. 2018;33(2):166-176.
6. Chen JT, Fagan MJ, Diaz JA, Reinert SE. Is treating chronic pain torture? Internal medicine residents’ experience with patients with chronic nonmalignant pain. Teach Learn Med. 2007;19(2):101-105.
7. Katz MH. Long-term opioid treatment of nonmalignant pain: a believer loses his faith [published correction appears in Arch Intern Med. 2010;170(20):1810]. Arch Intern Med. 2010;170(16):1422-1424.