THE CARLAT REPORT
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CURRENT COVERAGE OF TOPICS IN ADDICTION MEDICINE

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Kirk Brower, MD
Editor-in-Chief

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IN THIS ISSUE

Focus of the Month:
Pain and Addiction

Learning Objectives
After reading these articles, you should be able to:

1. Identify effective treatment options for patients with co-occurring pain and addiction.

2. Describe some of the challenges in both opioid and non-opioid treatment for pain.

3. Determine how to assess and treat psychogenic pain in psychiatric patients.

4. Summarize some of the current findings in the literature regarding psychiatric treatment.

Treating Chronic Pain When There's Addiction: A Primer

Michael McGee, MD
Chief medical officer, The Haven at Pismo, Avila Beach, CA. Author of The Joy of Recovery: A Comprehensive Guide to Healing from Addiction *(Union Square Publishing)*

Dr. McGee has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

In Summary

- Treating pain with co-occurring addiction involves minimizing suffering while continuing to help our patients stay in recovery.
- Chronic pain is multifaceted, so it's essential to do a careful and thorough assessment.
- Consider both non-opioid pharmacological and nonpharmacological therapies in pain management.

It can be challenging to manage chronic pain, even more so when our patients suffer from addiction. We can find ourselves walking a tightrope between the risk of relapse due to the inadequate treatment of pain, and the risk of relapse due to the use of opioid analgesics.

Since our mission is to minimize suffering and optimize functioning while helping our patients stay in recovery, this article will outline the general principles for achieving these goals in a pain management setting.

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Q&A With the Expert

Using Caution While Prescribing Opioids for Pain

Amy Bohnert, PhD

Associate professor of psychiatry at the University of Michigan, Investigator at The Center for Clinical Management Research, Department of Veterans Affairs, Ann Arbor, MI

Dr. Bohnert has disclosed that she has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

CATR: I know you've done a lot of research around overdose deaths, both intentional and unintentional, and how this may help psychiatrists more wisely prescribe opioids for pain. Can you start by giving us a little more background on that?
Dr. Bohnert: Sure. I'll start by talking a little about overdose deaths. The study that we did in the VA with mortality data shows there's a relationship between the dose of opioids a patient is prescribed and the patient's likelihood of dying by an unintentional overdose (Bohnert AS et al, *JAMA* 2011;305(13):1315–1321). What we found is that there's roughly a linear dose response curve, meaning simply that the greater the dose, the higher the risk of death.
CATR: Can you tell us what you specifically learned about the risk associated with higher doses of opioids?
Dr. Bohnert: Specifically, the risk of death from an overdose with patients prescribed at least 100 mg daily morphine equivalent is about 7 times higher than a patient prescribed less than 20 mg of morphine a day. This paper,

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Nature of chronic pain

There are three types of pain: nociceptive, neuropathic, and mixed. In acute pain, nociceptors send pain signals upon tissue injury. Neuropathic pain arises from dysfunction of the sensory nervous system, often due to sensory nerve injury. Mixed pain is a combination of nociceptive and neuropathic pain.

Chronic nociceptive pain can persist long after the healing of tissues. This appears to be due to autonomous neural signaling of sensitized nerve fibers. Alteration of inhibitory pain signaling may also play a role. For example, after suffering severe burns, some patients develop complex neuropathic pain syndromes.

Pain signals can be altered in the peripheral nerves, the spinal cord, the thalamus, and the cerebral cortex (Compton P et al. *Principles of Addiction Medicine, 5th ed.* Chevy Chase, MD: American Society of Addiction Medicine; 2014). This makes an accurate diagnosis of the chronic pain's source potentially important for treatment. For example, pain originating in peripheral nerves may respond best to electrical stimulation or acupuncture, while post-stroke pain that originates in the cerebral cortex will respond better to cortical interventions and cortex stimulation (Zaghi S et al, *J Pain Manag* 2009;2(3):339–352).

Psychosocial factors influence the perception and impact of chronic pain. For example, a positive outlook and family support can reduce both pain and disability (Flor H and Turk DC, *J Behav Med* 1988;11(3):251–265). Low self-efficacy is associated with greater depression, pain, and disability (Turk DC and Okifuji A, *J Consult Clin Psychol* 2002;70(3):678–690). Reinforcing pain behaviors—providing secondary gain—can also worsen a patient's symptoms and functioning. The benefits of pain (eg, relief from family obligations, medico-legal rewards) can both perpetuate disability and impede recovery (Dersh J et al, *J Occup Rehabil* 2004;14(4):267–279).

Preexisting psychiatric illnesses, including depression, anxiety, and PTSD, increase suffering due to pain and impair coping ability. (See https://bit.ly/2FUxIVu for a pain treatment improvement protocol.) Conversely, chronic pain often worsens psychiatric illness, creating a vicious cycle.

Additionally, chronic pain often causes depression, anxiety, insomnia, or impaired functioning. Like any stressor, chronic pain can also trigger relapse to addiction (Gourlay GL et al, *Pain Medicine* 2005;6(2):107–112). The interplay of addiction, other psychiatric illnesses, and chronic pain can make it challenging to assess and treat these conditions.

Assessment of patients with chronic pain

Since chronic pain is multifaceted, its assessment should be too. Be sure to obtain consent to speak to collateral providers and supports. You'll want to gather the findings of other clinicians and the observations and concerns of loved ones. Be sure to also check your state electronic prescription monitoring program to see whether the patient is being prescribed controlled substances. Ideally, you should try to obtain medical, psychiatric, and addiction treatment records from other clinicians.

After doing these things, you should assess the following:

- *Assess the nature of the pain.* Ask questions about onset, what the pain feels like, its severity, and what makes the pain worse (see box on page 3).
- *Assess how the pain impacts functioning.* Ask how the patient copes with it. How does the pain affect daily activities, including work, household responsibilities, socializing with friends, sex, and having fun?
- *Further explore how the pain makes the patient feel.* Does the patient feel irritable, frustrated, or hopeless? Be sure to ask how the pain is affecting sleep and mood. Listen for underlying negative beliefs about the pain, such as the idea that life is not worth living or that there is nothing that can be done about the situation. Is the patient willing to accept the pain and pursue a fulfilling life? Is there a sense that the pain can be addressed through the help of others? Degrees of acceptance and self-efficacy will inform and impact the treatment.
- *Ask about the impact of pain on a patient's recovery.* Is the patient sober? Having cravings? Is the patient adhering to a recovery program, or is pain getting in the way? Is the patient continuing to reach out to recovery supports, or retreating into isolation? If the patient is new to you, conduct a thorough substance use assessment, including details of current and past

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use, treatment history, and recovery history. Pay attention to factors that have sustained the patient's recovery and examine relapse history, taking note of factors that triggered relapse to addiction.

- *Assess all other co-occurring conditions and disorders.* Include other psychiatric illnesses, medical conditions, and neuropsychiatric impairments.
- *Assess environmental contingencies.* Does the family reinforce wellness behavior or illness behavior? Are there vocational, financial, or insurance/legal incentives or disincentives for being in pain? What will be the consequences of resuming healthy functioning? These factors can significantly impact pain severity and associated disability. Is the family concerned about the medication, opioids or otherwise, being prescribed to the patient?

In addition, conduct or obtain a physical exam. Look for relevant associated signs of a pain disorder and for signs of a substance use disorder, such as track marks, hepatomegaly, residuals of skin infections, and nasal and oropharyngeal pathology.

In your mental status exam, take note of whether the patient is focused on medications, particularly opioids. Look for somatic preoccupation. Assess both mood and the presence of suicidal ideation, intent, plans, and behaviors. Assess cognition, as impairments will affect the treatment.

Just as we assess our patients' "recovery capital" (social, cultural, emotional, financial, and occupational resources and supports), assess the patient's pain recovery capital. What environmental and social resources are available to promote wellness? Conversely, what are the patient's life stresses that impede healing from chronic pain?

After completing a thorough assessment, develop a formulation, or clinical understanding of the patient's difficulties. What are the patient's and family's overt and covert agendas? What are their impairments, and what factors contribute to those impairments? What are the patient's strengths and vulnerabilities? What resources can be brought to bear for the patient's healing? What stressors or other negative factors stand in the way of a successful outcome? A good formulation will make for a good treatment plan.

Assessing the Nature of Pain

*When assessing the nature of a patient's pain, Michael McGee, MD, recommends that you use the mnemonic "**OPQRST**," which stands for the following:*

"O" stands for onset: Was the pain gradual or sudden? What was the patient doing when it started?

"P" stands for provokes or palliates: Ask, "What situations cause the pain to get better or worse?"

"Q" stands for quality: Ask, "What does the pain feel like?" Let the patient attempt to describe the pain before giving options such as sharp, dull, or shooting.

"R" stands for radiates: Ask the patient to point to where the pain hurts the most, then ask, "Where does the pain go from there?"

"S" stands for severity: Ask how severe the pain is on a scale of 1–10, both when the pain is at its least severe and when it is at its worst. Ask whether the pain is constant or intermittent, and what the variation in severity is during a 24-hour cycle.

"T" stands for time: How long ago did the pain start? You also want to know the location(s) of the pain. If the patient claims to hurt "all over," ask the patient to point to where it hurts the most. Ask about prior pain assessments and the response to prior treatments, including complementary and alternative treatments.

Starting treatment

Treatment begins with an empathic connection. Try to make the patient feel understood and cared for. Since chronic pain can rarely be eliminated, it is important to communicate that you will be an ally throughout the patient's distress.

Begin treatment with education and negotiation of realistic treatment goals. Such goals include reduction of pain, maximization of functioning, and improvement in quality of life. I like to explain that there is a difference between suffering and distress. While the distress of pain can be reduced but not generally eliminated, suffering can be alleviated with a comprehensive, multimodal, biopsycho/social/spiritual approach.

Explain that pain is as much a psychological as a physical experience, and that it can be reduced by psychological and behavioral interventions. Patients need to understand that treating chronic pain is much more than taking a pill. They should also know that treating chronic pain generally takes a team: primary care providers, addiction specialists, pain clinicians, nurses, pharmacists, behavioral health clinicians, physical and occupational therapists, and alternative and complementary caregivers such as massage therapists and acupuncturists.

Reducing pain

You can frequently reduce pain using non-opioid analgesics. Acetaminophen should not exceed 4 g/day. With NSAIDs, be mindful of the risk of gastrointestinal bleeding and renal insufficiency. Combining or alternating acetaminophen with an NSAID and using them on a standing basis (not PRN) over a period of greater than 48 hours can optimize pain reduction (Altman RD, *Clin Exp Rheumatol* 2004;22(1):110–117). Serotonin-norepinephrine reuptake inhibitors (SNRIs) such as duloxetine and tricyclic antidepressants (TCAs) raise the pain threshold in the dorsal root ganglia and thus reduce pain levels.

Watch for anticholinergic side effects and orthostatic hypotension with TCAs (eg, confusion, constipation, and fall risk in the elderly). Due to the risk of cardiac conduction abnormalities, check an ECG when prescribing a TCA to someone over the age of 50. Antidepressants offer the obvious benefit of also treating co-occurring depression. Some anticonvulsants are indicated for treating fibromyalgia, migraine prophylaxis, and neuropathic pain.

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Q&A With the Expert

Assessing and Treating Psychogenic Pain

Howard Schubiner, MD

Director of the Mind Body Medicine Program at Providence Hospital, Southfield, MI.
Coauthor of the book Unlearn Your Pain: A 28-Day Process to Reprogram Your Brain.

Dr. Schubiner has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

CATR: To start, can you give us your take on the neurological process around pain? What's going on in the brain that causes a patient pain?

Dr. Schubiner: All pain is generated by what the neuroscientists call a salience network, or as I like to call it, the danger alarm mechanism. All pain is real. It's just a question of whether that pain is being triggered by a physical injury or by something else. Studies show that emotional injury activates the same areas of the brain as does physical injury (Kross E et al, *National Academies of Sciences* 2011;108:6270–6275). So, that gets us to the challenge of distinguishing between psychogenic pain and structurally induced pain.

CATR: Let's talk about psychogenic pain—that is, physical pain caused by emotional, behavioral, or mental health factors. How common is it?

Dr. Schubiner: I've found that a large proportion of patients with chronic pain do not have an identifiable structural cause for their pain. There's also a category of people with mixed pain, where there seems to be a combination of structural and psychogenic pain. Since going into this field, I've found it to be very common for people to have purely psychogenic symptoms. In fact, even with epilepsy, clinicians who routinely do video EEG monitoring find that up to 50% of patients with seizure disorders have psychogenic seizures (Reuber M, *Epilepsy and Behavior* 2008;12(4):622–635). About 24% of those referred for refractory seizures were found to have psychogenic non-epileptic seizures (PNES) after video/EEG monitoring; up to 50% of those with refractory status have PNES. That's an astoundingly high number. From my own clinical experience, I see a significant number of patients with chronic pain that can't be explained. I also see a number of patients I'm able to diagnose with purely psychogenic pain after connecting the pain to another disorder.

CATR: Can you tell us how to begin the process of assessing and treating a patient's pain?

Dr. Schubiner: I divide pain disorders into purely psychogenic, purely structural, and mixed. I believe this is a critical distinction. Obviously, we would treat psychogenic paralysis differently than we treat paralysis due to stroke or polio or Guillain-Barré syndrome. Typically, for psychogenic pain, what we see is that the pain often shifts from one location in the body to another. So, someone may at times have pain in the lower back, and at other times pain in the upper back. To me, that suggests that the brain is inducing that pain because of a non-structural cause. Chronic pain that spreads over time, for example starting in the lower back and then spreading up the spine, does not make sense neurologically. Psychogenic pain is commonly bilateral in distribution; it will start on one side and go to the other side in a mirror image fashion. The brain is very good at doing that. Obviously, some structural disorders can be bilateral too, but that's less common. So, in most patients with bilateral pain, I would suspect that the pain is psychogenic.

CATR: What are some of the triggers for psychogenic pain?

Dr. Schubiner: This is pain that can be triggered by stressful situations, and pain that goes away in situations where the brain is engaged or relaxed. So, for example, I had a recent patient who had 24/7 constant back pain, and when she went on vacation for a week, the pain completely disappeared. In another instance, I saw a patient who had a clinical diagnosis of repetitive strain injury in her wrist. The pain was worse Monday through Friday: The more she typed, the more she had hand pain. The clinical exam showed that there was no significant physical finding, suggesting that there wasn't any deformity, such as arthritis or inflammation. The patient noted, too, that she got pain on Sunday evening in anticipation of going to work the next day. For me, that was the clinical clue that led to the diagnosis of psychogenic pain, which then allowed her to fully recover following therapy. In these cases, though, we always need to look at imaging to first rule out structural problems.

CATR: Sounds like pain itself can be a defense mechanism against feeling certain emotions.

Dr. Schubiner: Yes. And oftentimes we see pain or other symptoms completely disappear on the spot by taking a mindfulness approach—we work to have patients observe symptoms without fear, without worry, and without danger, and oftentimes those symptoms will just literally turn off and evaporate on the spot.

CATR: It seems that, when there isn't a structural issue, many people don't want to be told that "it's all in their head," since that can make them feel that you are accusing them of causing their own pain. As part of all this, how do you talk to patients about pain disorders?

Dr. Schubiner: Saying "it's all in your head" is pejorative and a horrible thing to tell someone. When you say this, you're implying the pain isn't real, that the person is imagining or faking it, or that they are to blame for it. What

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many people want to say to the clinician who tells them that is, "*You* live in my body for a day and then tell me what it feels like!" So, here's a better approach: When I'm working with patients, step 1 is empathy. We need to show caring and compassion for patients and understand how severe their symptoms are. We need to connect with them on their level. After all, if they don't think you care, they are not going to trust what you tell them to do to alleviate their pain.

CATR: So, once you show patients you have empathy toward their pain, what do you do next?

Dr. Schubiner: For me, the second step is reviewing what's been tried. And typically, patients with chronic pain have tried frustrating and unsuccessful treatments. But listening to their previous experiences plants the seed that you empathize with them and reinforces that, even though there doesn't seem to be any structural problem, their pain is real. Listening to them earns their trust and confidence. The third step, then, is to explain pain.

CATR: What does explaining pain entail?

Dr. Schubiner: I explain pain using 3 brief stories. The first is of a man who was alone on a construction site who shot a nail into his hand by mistake and had zero pain. Even in the instance of an obvious physical injury, this story shows that the brain is powerful enough to control pain. The second story I tell is about a man written up in the *British Medical Journal* who jumped off the scaffolding on a construction site, impaling his foot on a nail that pierced all the way through his boot. This guy had severe pain, was rushed to the hospital, and given IV medication for pain. The nail was found to be precisely between his toes—there was no injury (Fisher JO et al, *BMJ* 1995:310–370).

CATR: Interesting. How do you reinforce with patients the "moral" of those stories?

Dr. Schubiner: I tell them it's important to recognize that the brain can create pain—real, severe pain, even in the absence of a physical injury. Explaining how the brain does that through a danger alarm mechanism will resonate with most patients.

CATR: How do you further connect patients to the idea that their pain might be psychogenic, and possibly related to stress or a traumatic experience?

Dr. Schubiner: The third story I tell them was told to me by another physician, who was in the Vietnam War as a young man. His company was ambushed, a lot of guys died, and he received a shrapnel injury to his leg. He had significant pain, and he was taken from the battlefield by helicopter to receive emergency treatment. I point out that—fortunately—his structural injuries eventually healed and he became pain-free. But almost 20 years later, a helicopter buzzed close by as he was walking down the street, and suddenly he got the exact same pain in his leg that he had had all those years earlier from the shrapnel. This story illustrates that neural pathways or neural circuits can learn pain, remember pain, and then activate pain due to a triggering mechanism. Those triggering mechanisms can be a variety of things, including foods, movements, lights, sounds, and stressful life events.

> **"We need to show caring and compassion for patients and understand how severe their symptoms are. After all, if they don't think you care, they are not going to trust what you tell them to do to alleviate their pain."**
>
> Howard Schubiner, MD

CATR: What do you do next?

Dr. Schubiner: The next step is to look for clues. Does the patient's pain fit into a pattern that could be placed clearly in the camp of psychogenic pain, structural pain, or mixed pain? Then I personalize that information and have a discussion with the patient about this idea of brain-induced pain. I provide resources to read and videos to watch, and I suggest that there is much more hope for people with brain-induced pain than there is for people with chronic, structural pain.

CATR: But doesn't everybody with chronic pain have a psychological component to their pain?

Dr. Schubiner: Of course. All pain, especially chronic pain, has a psychological component, and the methods we use can be helpful for people with mixed pain or even with purely structural pain—but only to a certain degree. Conversely, in people where we can clearly make the diagnosis of brain-induced pain, the chance of recovery becomes 100%—meaning the pain can actually be eliminated as opposed to coping with it and managing it with medications, which can be potentially problematic for those with existing substance use disorders. From our point of view, one of the problems in the field of chronic pain is the phrase "pain management." In the field, all pain is presumed to be structural or mixed, and therefore all pain—even if it's diagnosed as central pain such as fibromyalgia—is treated with a coping model rather than what could be a central pain recovery model (Litt MD and Tennen H, *Pain Manag* 2015;5(6):403–406).

CATR: Let's talk further, though, beyond musculoskeletal pain. For example, there is psychogenic pain that manifests itself through abdominal and nerve pain too, correct?

Dr. Schubiner: Of course, and through headaches as well. The data suggest that brain-induced pain and its associated conditions are very common. Roughly 40%–50% of people presenting to primary care offices have at least one medically unexplained symptom, and 25%–33% can be diagnosed with a somatoform disorder—in other words, they have symptoms that cannot be fully explained by any underlying general medical or neurologic condition (Haller H et al, *Deutsches Arz Int* 2015;112(16):279–287).

CATR: It seems like this is a good place to talk about how you approach treatment of psychogenic pain. What can you tell us here?

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Dr. Schubiner: I think it's important that patients first hear a clear, careful, and caring explanation of these disorders. This step can be quite difficult. We refer them to reading materials and videos to help them understand it, and sometimes it can take several weeks for people to grasp these ideas. We then use cognitive and behavioral interventions very similar to those employed in standard pain therapies, which include cognitive behavioral therapy, mindfulness, acceptance and commitment therapy, and other modalities.

CATR: Can you give us a couple of high-level examples of how you approach those therapies?

Dr. Schubiner: Sure. I like to use words that empower patients to not shrink in the wake of their symptoms, to remind themselves that they are healthy and not damaged, and to be able to reduce their fear in the wake of having symptoms. We also challenge some of the triggers of symptoms by actively engaging in specific movements or activities, especially those that have caused symptoms in the past. But we do this with the mindset of, "I am not damaged and I will be fine." Mindfulness meditation is used as an adjunct in this situation, and again what we have found is that mindfulness is actually much more effective in a setting of, "I'm not damaged," as opposed to a setting of, "I'm damaged and I'm coping as best I can with these symptoms."

CATR: What are the final steps in your treatment strategy?

Dr. Schubiner: We go through emotional processing. Not all patients need this part of the approach, but some do, and it is well-known that people with adverse childhood events have much higher rates of chronic pain and other disorders later in life. This involves asking patients to experience, express, and release emotions that may have been avoided earlier in life, including anger, guilt, sadness, and compassion. Part of this treatment is to enhance compassion for oneself and forgiveness for the self and others. The final component of the treatment is to make necessary changes in one's life as they are identified. Some people are in difficult situations in relation to family members, work, etc—dealing with those challenges can often be an important part of the treatment. Overall, all the treatment is directed to decreasing fear, and ultimately toward helping patients with their pain.

CATR: I'd like to also specifically ask about patients who are either on opioids or have an opioid use disorder, and are also coping with psychogenic pain. Can you talk about how to approach treatment in that scenario?

Dr. Schubiner: People who are on opioids often have a difficult time reducing or eliminating those doses. The primary reason for this difficulty is fear of increased pain. And when patients are presented with the ultimatum of reducing opioid doses, oftentimes that further activates the danger alarm mechanism in the brain and produces more pain. That becomes counterproductive when trying to get people off of these medications. So, with people who are on opioids and in whom I've diagnosed a brain-induced disorder, I don't suggest reducing the dose at all. First, I work on reducing or eliminating the pain, and once that occurs, it's much easier to reduce the doses or wean off of the opioid medications.

CATR: So, the step-by-step treatment that you've outlined can actually take place while someone is still taking the opioids or has another co-occurring substance use disorder?

Dr. Schubiner: Yes, in my experience that's been the case.

CATR: Thank you for your time, Dr. Schubiner.

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as well as additional similar research findings, led to a CDC guideline recommending against prescribing high doses of opioids (see: https://www.cdc.gov/drugoverdose/prescribing/guideline.html).

CATR: So, is there a consensus on what is a safe dose of opioids to manage chronic pain?

Dr. Bohnert: What we found when we did our analysis was that there really was no dose that is completely safe, and there are patients who die of opioid overdoses across the full spectrum of dosages (Bohnert AS et al, *Med Care* 2016;54(5):435–441). So, there isn't a point at which you can say, "oh, as long as the patient's not above 20 morphine-equivalent milligrams, that means there's no problem." There's an overdose risk at every level. But in the interest of trying to encourage physicians to prescribe lower, less risky doses, we determined through the research that less than 50 morphine-equivalent mg per day should be the recommendation put forth in the new CDC guideline. Above 50 mg, the rates of overdose were considerably higher.

"One thing that would be particularly relevant to mental health practitioners is to avoid concurrently prescribing benzodiazepines and opioids. In our VA study, about 50% of those who died from an overdose were on both opioids and benzodiazepines."

Amy Bohnert, PhD

CATR: Is there anything else we should know about the CDC guideline?

Dr. Bohnert: Yes. We need to keep in mind that the CDC guideline overall really addresses the question, "How do we approach pain treatment going forward?" What it did not intend to answer was, "What do we do with the cohort of people who were prescribed long-term opioids before the guideline was released?" So, the guideline is more about taking a proactive approach going forward. It also left a lot of unanswered questions, which we'll need to answer through future research. For example, when is it appropriate to have patients de-intensify or go off opioids? Until we get those answers, it might be a struggle for clinicians dealing with issues of opioid pain management treatment across all clinical settings. The CDC, though, has offered some guidance here (see: https://bit.ly/2oHXK4C).

CATR: Can you tell us more about what you've learned while researching deaths associated with intentional vs unintentional opioid overdose?

Dr. Bohnert: We were able to cross-match between medical records data and mortality data, and we specifically looked at the presence of mental health conditions as indicated by diagnostic codes (Bohnert AS et al, *Inj Prev* 2013;19(5):326–330). What we found was that the risk of intentional overdose (eg, suicide), unintentional overdose, and what we termed "undetermined intent" was associated with essentially every mental health diagnosis group in the study. Not surprisingly, people with a diagnosis of substance use disorder had a stronger association with unintentional overdose deaths and suicide. The undetermined deaths were higher across all the diagnoses, which suggests there are patients who are struggling with a lot of comorbidity—that is, their psychiatric and substance use disorder history makes it more difficult to determine whether the overdose was intentional or unintentional.

CATR: What else can we as psychiatrists and addiction treatment specialists learn from these new CDC guidelines?

Dr. Bohnert: One thing that would be particularly relevant to mental health practitioners is to avoid concurrently prescribing benzodiazepines and opioids. In our VA study, about 50% of those who died from an overdose were on both opioids and benzodiazepines. I think this makes it very important to decide, on a patient-by-patient basis, which of the treatments to prioritize. More research likely needs to be done here, but for now it's a good idea to proceed with caution when using both medications.

CATR: Do you think overprescribing of opioids is still a problem these days?

Dr. Bohnert: Yes, I think it is still happening to some degree. Some of that is based on consumption data, and we know that—when people get prescribed opioids for acute pain—the common thing to do is to give them more than what they'll actually need (Bartels K et al, *PLoS One* 2016;11(1):e0147972). That's usually to avoid patients calling back into the office to ask for a refill when they're still experiencing pain. It's challenging, though, because physicians naturally want the patient to feel like the pain is taken care of, and not being undertreated. But this overprescribing does seem to be more common in an acute pain rather than chronic pain context. With chronic pain prescribing, it's easier to tell the patient, "I'm going to give you the appropriate amount of pills that you'll need until I see you in a month, and I won't be able to give you any extra."

CATR: I also know that the guidelines speak to screening or diagnosing an opioid use disorder in patients with chronic pain. Can you elaborate on that part?

Dr. Bohnert: There are a couple of things to be thinking about in terms of screening for opioid use problems. If we're talking about chronic pain patients, the current opioid misuse measure (COMM) is probably my preferred measure for taking a snapshot of someone's current level of opioid use, and it can pick up on change over time. It includes a brief patient assessment questionnaire (see: https://bit.ly/2IggZbU), and studies have shown the COMM to be a reliable and valid screening tool to help detect aberrant drug-related behavior among chronic pain patients (Butler SF et al, *Clin J Pain* 2010;26(9):770–776). Another questionnaire assessment tool to consider is the Screener and Opioid Assessment for Patients with Pain (SOAPP). It measures differently than the COMM. The way I would describe the difference is that SOAPP (see: https://www.nhms.org/sites/default/files/Pdfs/SOAPP-5.pdf) is better for predicting at the start of treatment if a patient might be predisposed to developing an opioid use disorder.

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Expert Interview – Using Caution While Prescribing Opioids for Pain
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CATR: That's good advice on screening. I'd like to switch gears a little and ask you what you're seeing in the literature as it relates to non-opioid approaches to treating pain. What are you learning here?

Dr. Bohnert: Just recently, *JAMA* published a study led by Erin Krebs and colleagues at the Minneapolis VA, where they found that opioid and non-opioid medications were equally effective for treating chronic back, hip, or knee osteoarthritis pain. In fact, that study even showed that those on opioids did a little bit worse. They randomized people on immediate release morphine, oxycodone, or hydrocodone/acetaminophen in the opioid group. For the non-opioid group, the first step was acetaminophen (paracetamol) or a nonsteroidal anti-inflammatory drug (Krebs EE et al, *JAMA* 2018;319(9):872–882). I think that's a landmark study. Previously, I had not seen any kind of comprehensive head-to-head trial of opioids compared to alternatives that carry a lot less risk. So, we'll still see how things play out over the next couple of years, but I think that *JAMA* study has potential to further reinforce the new CDC guideline around deciding when to start opioid pain therapy. Certainly it's more evidence that fewer patients may benefit from opioid therapy than we once thought.

CATR: Those are definitely interesting findings. What else have you seen in the literature related to alternatives to opioids?

Dr. Bohnert: Another paper that came out in 2016, which was shortly after the CDC guideline, involved a head-to-head comparative effectiveness study of cognitive behavioral therapy (CBT) and mindfulness for chronic pain. The researchers found that both therapies were equally good, and that both were better than receiving nothing (Cherkin DC et al, *JAMA* 2016;315(12);1240–1249). I think that's also a really interesting study. It shows that we have a great opportunity to give patients a choice about which of those modalities they think is a better match for them.

CATR: Since it's related to the topic, what are your thoughts on medication-assisted treatment (MAT) when it comes to opioid use disorders that develop after treating someone with chronic pain?

Dr. Bohnert: In the CDC guideline, there's a recommendation for using MAT specifically for patients who have developed an opioid use disorder after being on chronic opioid therapy. A consideration, too, is that there's some evidence of buprenorphine-naloxone (Suboxone) having some analgesic properties that could allow it to treat pain as well as opioid use disorder, but that evidence is somewhat limited. I think in the meantime it's important that Suboxone not be thought of as the whole of a patient's pain treatment. This gets to a broader point across all addictions—with someone who has comorbid pain and addiction, it's really important to be treating both issues. After all, there's evidence that patients are more likely to relapse if their chronic pain goes untreated.

CATR: So maybe this is where the buprenorphine comes in, but in terms of treating people who have both an opioid use disorder and moderate to severe and chronic pain, did the CDC guideline address that issue?

Dr. Bohnert: Yes. The primary way the CDC guideline addressed it was by providing a guidance around offering Suboxone. So, for patients with an opioid use disorder and chronic pain, it's definitely appropriate to consider that treatment.

CATR: What are some additional non-opioid treatments you'd recommend for chronic pain?

Dr. Bohnert: There are a lot of non-pharmacologic modalities that can be prioritized as treatment options. For example, there's yoga and other exercise-based treatments. There's CBT, mindfulness, acceptance and commitment therapy, and physical therapy. Obviously, insurance coverage for the non-pharmacologic treatments can be an issue, so there is a little bit of swimming against the tide to get access to those for a patient. But even some free programs around pain self-management, such as those for mindfulness or relaxation, are certainly better than nothing. I would say it's important not only that we help make sure patients' pain is addressed, but also that we always take their pain seriously.

CATR: Well, this has been a very informative interview. Is there anything you'd like to leave us with on the subject?

Dr. Bohnert: Something that's really important to me in my work now is to think about how we address access to MAT. Many patients don't have this. Either they live somewhere where there are very few providers, or their insurance doesn't give them access to providers who are local, or there are long waiting lists at the local treatment programs. So, I think that's something that we will need to continue working on as a clinical community.

CATR: Thank you for your time, Dr. Bohnert.

❖ ❖ ❖

Research Updates

ALCOHOL

Prevalence of Fetal Alcohol Spectrum Disorder

REVIEW OF: May PA et al, *JAMA* 2018;319(5):474–482

New evidence suggests that the prevalence of fetal alcohol spectrum disorder is higher than previously documented. In this study, prevalence estimates were derived from 13,146 first-grade children in four U.S. communities between 2010 and 2016. The authors provide both conservative estimates (1%–5%) and less conservative estimates (3%–10%) of fetal alcohol spectrum disorders, which are higher than previously reported (eg, 1%–2%).

The study used active-case ascertainment, which the authors assert is a more reliable approach for identifying this cluster of disorders (eg, fetal alcohol syndrome, partial fetal alcohol syndrome, and alcohol-related neurodevelopment disorder). With active-case ascertainment, surveillance personnel are trained to conduct research by reviewing data from all areas of a hospital that come in contact with a neonate, instead of limiting themselves to the neonatal intensive care and labor and delivery units.

Furthermore, standardized consensus criteria were employed to classify cases (see: https://www.cdc.gov/ncbddd/fasd/diagnosis.html). Assessments included four relevant domains: growth, dysmorphology, neurodevelopment, and prenatal alcohol exposure (the latter assessed during maternal interviews).

During this time period, 222 children were identified as having fetal alcohol spectrum disorder. Notably, only two of these children had been previously diagnosed. Using the more conservative approach, the prevalence rates of fetal alcohol spectrum disorders across the four sites ranged from 11.3 (95% CI, 7.8–15.8) to 50.0 (95% CI, 39.9–61.7) per 1,000 children. This corresponds to a range of approximately 1%–5%, the latter of which is higher than previous published estimates. The less conservative estimates that were reported in this study peaked at 98.5 per 1,000 children (nearly 10%) at one site.

CATR'S TAKE

According to this new research, fetal alcohol spectrum disorders are not rare events in the US, which suggests we need to improve our ability to detect these cases. Given the negative (and preventable) consequences associated with fetal alcohol spectrum disorders (eg, poor academic achievement, mental health disorders), *CATR* recommends proactive education on the adverse consequences of drinking alcohol during pregnancy, in addition to enhanced prevention and intervention efforts. Also, support services should be provided for individuals affected by this condition, with the goal of improving their long-term prognosis and enhancing their quality of life.

—Christian J. Teter, PharmD, BCPP. Dr. Teter has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

ALCOHOL

Is Varenicline Effective for Alcohol Use Disorder?

REVIEW OF: O'Malley S et al, *JAMA Psychiatry* 2018;75(2):129–138

Acting on the nicotinic acetylcholine receptors, varenicline (Chantix) is an FDA-approved treatment for smoking cessation. These receptors are implicated in both nicotine and alcohol reward pathways, so could varenicline also be helpful for treating alcohol use disorder (AUD)? So far, the evidence has been mixed, but some studies have shown a greater benefit of varenicline in those who use both alcohol and cigarettes, compared to those who just use alcohol.

This 16-week study was a phase 2, randomized, double-blind, placebo-controlled trial comparing the effects of varenicline and medical management to medical management plus placebo for treatment of AUD. The 131 participants recruited (including 39 women) met DSM-IV-TR criteria for alcohol dependence and smoked at least 2 days a week. The intervention group was given varenicline titrated up to 1 mg twice a day, and both groups were seen for 12 medical management sessions for AUD, which is a behavioral intervention used by medical professionals to support medication adherence (4 sessions) and use strategies for achieving drinking goals (8 sessions).

The primary outcomes were reduction in drinking by percentage of heavy drinking days (PHDD) and no heavy drinking days (NHDD), defined as ≥ 5 standard drinks a day for men or ≥ 4 for women. One standard drink equaled a 12-ounce beer with an alcohol content of 5%, 5 ounces of wine (12% alcohol), or 1.5 ounces of distilled spirits (40% alcohol). Secondary outcomes were prolonged abstinence (28 days) from smoking, confirmed by plasma cotinine levels < 6 ng/mL.

The results of the primary outcome, PHDD, showed no significant difference in the overall sample between those on varenicline or placebo. However, there was a significant difference between the response of men and women in the study. PHDD in men showed a greater (but still non-significant) reduction than women, and the NHDD in men was nearly significant—29% on varenicline had NHDD vs 6% for placebo (95% CI, 0.22–1.03). Smoking outcomes showed a significant difference in prolonged abstinence from smoking for those on varenicline—13% vs 0% (P = .003). The only significantly different side effect was more abnormal dreaming in the varenicline group (43.8% vs 22.4%), which was experienced more often by women than men—women taking varenicline were 35% more likely than men to report this complaint.

Three adverse events happened in the varenicline group: an admission to alcohol rehabilitation, a hospitalization for suicidal ideation, and another hospitalization for blood pressure monitoring. Two adverse events happened with placebo: psychiatric hospitalization in one, and hospitalization for an infection in another. Women on varenicline were more likely to report abnormal dreams and to reduce or discontinue the medication than either men or women on placebo.

CATR'S TAKE

While the results are not robust, they point to a greater benefit in men with AUD than in women. However, the small

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Research Updates

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number of women in the study limits this conclusion, and it could be that women don't tolerate treatment doses of varenicline as well. More research is needed to look into these differences. Another take-home point is that, even without any other smoking cessation interventions, varenicline helped with prolonged abstinence from smoking.

—Thomas Jordan, MD. Dr. Jordan has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

OPIOIDS

Guidelines for Switching From Methadone to Buprenorphine

REVIEW OF: Lintzeris N et al, *J Addict Med* 2018. doi:10.1097/ADM.0000000000000396

Recent guidelines published by the American Society of Addiction Medicine and nationally in Australia provide support for transferring patients from methadone to buprenorphine-naloxone (BNX). Patients may switch, thinking BNX is easier to discontinue or because of methadone side effects. The transition can be complicated by relapses or precipitated withdrawal when starting BNX. To minimize adverse events, the Australian guidelines recommend the following:

1. Consider inpatient treatment for patients with significant medical comorbidities, unstable social conditions, or for those transferring from high methadone doses (> 50 mg/day)
2. Gradually reduce methadone until the patient experiences mild to moderate opioid withdrawal symptoms between doses
3. Stop methadone and begin monitoring regularly for opioid withdrawal, using measures such as the Clinical Opioid Withdrawal Scale (COWS)
4. Start low-dose BNX at 2 mg, at least 24 hours after the last dose of methadone and after the patient experiences moderate opioid withdrawal (COWS score > 12), monitoring hourly afterwards for precipitated withdrawal
5. Administer 6 mg after 1 hour; additional doses, 4–8 mg, are symptom-triggered
6. On successive days: BNX dosage = the previous day's dose plus additional symptom-triggered doses

Lintzeris and colleagues studied the clinical feasibility of these guidelines. Involving 4 Australian specialist addiction centers, they conducted a prospective cohort study. They reviewed medical records. Outcomes assessed included guideline feasibility, transfer practices, and patient responses.

In all, 33 adult participants transferred, 9 from low-dose (LD) methadone (< 30 mg/day), 9 from medium-dose (MD) methadone (30–50 mg/day), and 15 from high-dose (HD) methadone (> 50 mg/day). Most HD transfers occurred in inpatient settings (93%), while most MD/LD transfers occurred in outpatient settings (67%). Inpatient stays were 2.2 days on average. Seventy percent of transfers were consistent with the guidelines. Most patients stabilized their BNX dose by day 3, with 96% using ≥ 12 mg/day. Overall, 79% (26/33) were still on BNX treatment at day 7 and were considered to have successfully transferred.

Three patients experienced precipitated withdrawal, all in the HD group, all returning to methadone. Three patients resumed methadone due to anxiety and poor sleep with BNX. One participant relapsed and used heroin for several days before resuming methadone.

CATR'S TAKE

Although this was a small sample, the findings are useful. They suggest most patients can successfully transfer from methadone to BNX when using the guidelines. Those transferring from HD methadone require inpatient settings and specialist supervision, while two-thirds of MD/LD methadone transfers may be suitable for outpatient clinics. Since all those patients failed transfer, it is important to avoid precipitated withdrawal.

—Rehan Aziz, MD. Dr. Aziz has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

Treating Chronic Pain When There's Addiction: A Primer

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Be mindful that gabapentin and pregabalin (a Schedule V controlled substance) can be misused and that discontinuation can cause withdrawal symptoms. Carefully monitor the use of these medications. Topical analgesics, including topical NSAIDs, capsaicin, and lidocaine, provide treatment of localized superficial pain with minimal systemic side effects.

Muscle relaxants, benzodiazepines, and THC are generally not recommended for treating chronic pain, especially in patients with a vulnerability to addiction. Cannabidiol, which is non-psychoactive, may be helpful for some patients, particularly for central neuropathic pain, inflammatory, and cancer pain (Russo EB, *Ther Clin Risk Manag* 2008;4(1):245–259); however, more research is required and it lacks FDA approval.

Non-pharmacological approaches

Cognitive behavioral therapy (CBT) addresses negative cognitions and unhelpful pain behaviors, including avoidance and isolation. CBT can reduce pain and associated distress, disability, depression, anxiety, and catastrophizing. It can also improve functioning, sleep, and coping (Vitiello MV et al, *J Clin Sleep Medicine* 2009;5(4):255–362).

Mindfulness approaches, especially mindfulness-based stress reduction, enhance distress tolerance through acceptance and nonjudgment. They diminish the anxiety and depression that can arise as distress-avoidant responses to pain. Practicing the acceptance of pain can help reduce the suffering associated with it.

A word about opioid treatment

Research suggests that chronic opioid treatment fares no better than long-term

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CE/CME Post-Test

This CME test is only available to active subscribers. Tests must be completed within a year from each issue's publication date. If your subscription expires before that date, you will not have access to the test until your subscription is renewed. To earn CME or CE credit, you must read the articles and then take the post-test at www.TheCarlatReport.com. You must answer 75% of the questions correctly to earn credit. You will be given two attempts to pass the test. As a subscriber to *CATR*, you already have a username and password to log onto www.TheCarlatReport.com. To obtain your username and password, please email info@thecarlatreport.com or call 978-499-0583.

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Below are the questions for this month's CE/CME post-test. This page is intended as a study guide. Please complete the test online at www.carlataddictiontreatment.com. Note: Learning objectives are listed on page 1.

1. In addition to the risk of triggering relapse in patients with opioid use disorders, opioid treatment rarely shows more than a ____ reduction in pain beyond 18 months. (LO #1)

   [ ] a. 10% [ ] b. 25% [ ] c. 33% [ ] d. 50%

2. What is the approximate risk of overdose death for patients prescribed at least 100 mg of morphine per day compared to patients prescribed less than 20 mg of morphine per day? (LO #2)

   [ ] a. Both doses have the same risk of death
   [ ] b. 3 times higher
   [ ] c. 7 times higher
   [ ] d. 11 times higher

3. According to Dr. Schubiner, which of the following is characteristic of psychogenic pain? (LO #3)

   [ ] a. Pain that begins from nerve roots in the spinal cord and extends simultaneously to nerve endings down both lower limbs
   [ ] b. Localized burning, throbbing, or stabbing pain that occurs after a viral infection
   [ ] c. Pain along one side of the body
   [ ] d. Pain that often shifts from one location in the body to another

4. A 2018 study found that opioid medication is more effective than non-opioid medication for treating chronic back, hip, or knee osteoarthritis pain. (LO #2)

   [ ] a. True [ ] b. False

5. According to a 2018 study, the prevalence of fetal alcohol spectrum disorder in the US is: (LO #4)

   [ ] a. 0.1%–0.5% [ ] b. 0.5%–3% [ ] c. 1%–5% [ ] d. 2%–7%

6. According to Dr. McGee, an optimal way to reduce pain using non-opioid analgesics is to combine or alternate acetaminophen with an NSAID on a standing basis over a period of greater than 48 hours. (LO #1)

   [ ] a. True [ ] b. False

7. According to Dr. Bohnert, which of the following statements about non-opioid treatment of pain is true? (LO #2)

   [ ] a. Nonpharmacologic modalities are most effective for patients with pre-existing depression prior to experiencing chronic pain
   [ ] b. Cognitive behavioral therapy and mindfulness are equally effective non-pharmacologic treatments for chronic pain
   [ ] c. Approximately 20% of patients using yoga and other exercise-based treatments for chronic pain benefit from the placebo effect
   [ ] d. Cognitive behavioral therapy is the only non-pharmacologic modality shown to be effective for chronic pain treatment

8. According to a 2018 study, varenicline was more effective at reducing heavy drinking in male participants than female participants. (LO #4)

   [ ] a. True [ ] b. False

THE CARLAT REPORT:
ADDICTION TREATMENT

P.O. Box 626
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This Month's Focus:
Pain and Addiction

Next month in *The Carlat Addiction Treatment Report:*
Adolescent Addiction

Treating Chronic Pain When There's Addiction: A Primer

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non-opioid treatment of moderate to severe chronic pain due to osteoarthritis (Krebs E et al, *JAMA* 2018;319(9):872–882). Pain specialists should only initiate opioid pharmacotherapy as a last resort, when other interventions have failed, and only after a careful consideration of the potential risks and benefits.

Opioid treatment rarely shows more than a one-third reduction in pain beyond 18 months and poses the risk of triggering relapse in patients with opioid use disorder and other addictions (Reid MC et al, *J Gen Internal Medicine* 2002;17(3):173–179). Opioids may be necessary in extreme cases, however, and they should not be totally ruled out simply because your patient has an addiction. Buprenorphine can be considered for patients with both chronic pain and moderate to severe opioid use disorders. Any patient with addiction to opioids will require careful monitoring, and many patients will not benefit from prolonged opioid therapy.

CATR VERDICT: In treating chronic pain and addiction, work to improve functioning, reduce pain, and ease psychological suffering. Integrate the treatment of pain and other comorbidities, including addictions and other psychiatric illnesses. Combine non-opioid pharmacological and nonpharmacological therapies, collaborating as part of a team with other caregivers. As always, be wary of the risk of relapse, and consider the potential role of buprenorphine.