

CHARLES REZNIKOFF, MD, FACP

Addiction Medicine, Department of Medicine,
Hennepin County Medical Center, Minneapolis, MN;
Assistant Professor of Medicine, University of
Minnesota, Minneapolis

How acute pain leads to chronic opioid use

MARY, AGE 38, was hospitalized for acute cholecystitis requiring laparoscopic surgery. Her hospital course was uneventful. At the time of discharge, I, her inpatient doctor, prescribed 15 hydrocodone tablets for postoperative pain. I never saw her again. Did she struggle to stop taking the hydrocodone I prescribed?

Heather is a 50-year-old patient in my addiction medicine clinic who developed opioid use disorder while being treated for chronic pain. After much hardship and to her credit, she is now in long-term remission. Did her opioid use disorder start with an opioid prescription for an accepted indication?

The issues Mary and Heather face seem unrelated, but these 2 patients may be at different time points in the progression of the same disease. As a hospitalist, I want to optimize the chances that patients taking opioids for acute pain will be able to stop taking them.

■ CHRONIC USE VS OPIOID USE DISORDER

There is a distinction between chronic use of opioids and opioid use disorder. The latter is also known as addiction.

Patients who take opioids daily do not necessarily have opioid use disorder, even if they have physiologic dependence on them. Physiologic opioid dependence is commonly confused with opioid use disorder, but it is the expected result of regularly taking these drugs.

Opioid use disorder is a chronic disease of the brain characterized by loss of control over opioid use, resulting in harm. The *Diagnostic and Statistical Manual*, fifth edition, excludes physiologic dependence on opioids (tolerance

and withdrawal) from its criteria for opioid use disorder if the patient is taking opioids solely under medical supervision.¹ To be diagnosed with opioid use disorder, patients need to do only 2 of the following within 12 months:

- Take more of the drug than intended
- Want or try to cut down without success
- Spend a lot of time in getting, using, or recovering from the drug
- Crave the drug
- Fail to meet commitments due to the drug
- Continue to use the drug, even though it causes social or relationship problems
- Give up or reduce other activities because of the drug
- Use the drug even when it isn't safe
- Continue to use even when it causes physical or psychological problems
- Develop tolerance (but, as noted, not if taking the drug as directed under a doctor's supervision)
- Experience withdrawal (again, but not if taking the drug under medical supervision).

■ WHY DO SOME PATIENTS STRUGGLE TO STOP TAKING OPIOIDS?

Studying opioid use disorder as an outcome in large groups of patients is complicated by imperfect medical documentation. However, using pharmacy claims data, researchers can accurately describe opioid prescription patterns in large groups of patients over time. This means we can count how many patients keep taking prescribed opioids but not how many become addicted.

In a country where nearly 40% of adults are prescribed an opioid annually, the question is not why people start taking opioids, but why some have to struggle to stop.² Several recent studies used pharmacy claims data to identify

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factors that may predict chronic opioid use in patients prescribed opioids for acute pain. The findings suggest that we can better treat acute pain to prevent chronic opioid use.

We don't yet know how to protect patients like Mary from opioid use disorder, but the following 3 studies have already changed my practice.

HIGHER TOTAL DOSE MEANS HIGHER RISK

Shah A, Hayes CJ, Martin BC. Characteristics of initial prescription episodes and likelihood of long-term opioid use—United States, 2006–2015. *MMWR Morb Mortal Wkly Rep* 2017; 66(10):265–269.

Shah et al³ reported a study of nearly 1.3 million opioid-naïve patients who received opioid prescriptions. Of those prescribed at least 1 day of opioids, 6% were still taking them 1 year later, and 2.9% were still taking them 3 years later.

Opioid exposure in acute pain was measured in total “morphine milligram equivalents” (MME), ie, the cumulative amount of opioids prescribed in the treatment episode, standardized across different types of opioids. We usually think of exposure in terms of how many milligrams a patient takes per day, which correlates with mortality in chronic opioid use.⁴ But this study showed a linear relationship between *total* MME prescribed for acute pain and ongoing opioid use in opioid-naïve patients. By itself, the difference between daily and total MME made the article revelatory.

But the study went further, asking how much is too much: ie, What is the cutoff MME above which the patient is at risk of chronic opioid use? The relationship between acute opioid dose and chronic use is linear and starts early. Shah et al suggested that a total threshold of 700 MME predicts chronic opioid use—140 hydrocodone tablets, or 1 month of regular use.³

Many doctors worry that specific opioids such as oxycodone, hydromorphone, and fentanyl may be more habit-forming. Surprisingly, this study showed that these drugs were associated with rates of chronic use similar to those of other opioids when they controlled for potency.

Bottom line. Total opioid use in acute pain was the best predictor of chronic opioid use, and it showed that chronicity begins earlier than thought.

DON'T BE A 'HIGH-INTENSITY' PRESCRIBER

Barnett ML, Olenski AR, Jena AB. Opioid-prescribing patterns of emergency physicians and risk of long-term use. *N Engl J Med* 2017; 376(7):663–673.

Barnett et al⁵ analyzed opioid prescribing for acute pain in the emergency department, using Medicare pharmacy data from 377,629 previously opioid-naïve patients. They categorized the emergency providers into quartiles based on the frequency of opioid prescribing.

The relative risk of ongoing opioid use 1 year after being treated by a “high-intensity” prescriber (ie, one in the top quartile) was 30% greater than in similar patients seen by a low-intensity prescriber (ie, one in the bottom quartile). In addition, those who were treated by high-intensity prescribers were more likely to have a serious fall.

In designing the study, the authors assumed that patients visiting an emergency department had their doctor assigned randomly. They controlled for many patient variables that might have confounded the results, such as age, sex, race, depression, medical comorbidities, and geographic region. Were the higher rates of ongoing opioid use in the high-intensity-prescriber group due to the higher prescribing rates of their emergency providers, or did the providers counsel patients differently? This is not known.

Bottom line. Different doctors manage similar patients differently when it comes to pain, and those who prescribe more opioids for acute pain put their patients at risk of chronic opioid use and falls. I don't want to be a high-intensity opioid prescriber.

SURGERY AND CHRONIC OPIOID USE

Brummett CM, Waljee JF, Goesling J, et al. New persistent opioid use after minor and major surgical procedures in US adults. *JAMA Surg* 2017; 152(6):e170504.

Brummett et al⁶ examined ongoing opioid use after surgery in 36,177 opioid-naïve patients and in a nonsurgical control group. After 3 months, 6% of the patients who underwent surgery remained on opioids, compared with only 0.4% of the nonsurgical controls. Whether the surgery was major or minor did

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not affect the rate of postoperative opioid use.

Risk factors for ongoing opioid use were preexisting addiction to anything (including tobacco), mood disorders, and preoperative pain disorders. These risk factors have previously been reported in nonsurgical patients.⁷

Brummett et al speculated that patients are counseled about postoperative opioids in a way that leads them to overestimate the safety and efficacy of these drugs for treating other common pain conditions.⁶

Bottom line. Patients with mental health comorbidities have a hard time stopping opioids. The remarkable finding in this study was the similarity between major and minor surgery in terms of chronic opioid use. If postoperative opioids treat only the pain caused by the surgery, major surgery should be associated with greater opioid use. The similarity suggests that a mechanism other than postoperative pain confers risk of chronic opioid use.

■ THINKING ABOUT OPIOIDS

Collectively, these articles describe elements of acute pain treatment that correlate with chronic ongoing opioid use: a higher cumulative dose,³ being seen by a physician who prescribes a lot of opioids,⁵ undergoing surgery,⁶ and psychiatric comorbidity.⁶ They made me wonder if opioid use for acute pain acts as an inoculation, analogous to inoculating a Petri dish with bacteria. The likelihood of chronic opioid use arises from the inoculum dose, the host response, and the context of inoculation.

These articles do not show how patients taking opioids chronically for pain become addicted. Stumbo et al⁸ interviewed 283 opioid-dependent patients and identified 5 pathways to opioid use disorder, 3 of which were related to pain control: inadequately controlled chronic pain, exposure to opioids during acute pain episodes, and chronic pain in patients who already had substance use disorders. Brat et al⁹ recently estimated the risk of opioid use disorder after receiving opioids postoperatively to be less than 1%, but it increased dramatically with duration of opioid treatment.

Estimates of the prevalence of opioid use disorder in patients with chronic pain vary, but it is substantial. Vowles et al,¹⁰ in a meta-analysis, put the number at about 11% of pa-

Take-home points

Several recent studies used pharmacy claims data to find factors that may predict chronic opioid use in patients given opioids for acute pain. The findings suggest how doctors can better treat acute pain to prevent chronic opioid use.

Chronic opioid use for pain is an adverse and preventable outcome but is not synonymous with opioid use disorder.

Even a sincere patient with a "legitimate" source of pain may struggle to stop taking opioids after the pain resolves.

The initial opioid dose, the patient's mental health comorbidities, and the practice of the opioid prescriber correlate with ongoing opioid use for pain.

tients on chronic opioid therapy. Others say it is higher: for every 5 Americans who take opioids for pain without addiction, 1 becomes addicted.^{2,11} Though opioid use disorder is a serious adverse outcome of opioid prescribing, it occurs in only a minority of patients taking daily opioids. These studies demonstrate that chronic opioid use without addiction is also an important undesirable outcome.

A patient who fills an opioid prescription does not necessarily have chronic pain. Nor do all patients with chronic pain require an opioid prescription. These studies did not establish whether the patients had a pain syndrome. In practice, we call our patients who chronically take opioids our "chronic pain patients." But 40% of Americans have chronic pain, while only 5% take opioids daily for pain.^{11,12}

We assume that those taking opioids have the most severe pain. But Brummett et al suggested that continued opioid use is predicted less by pain and more by psychiatric comorbidity.⁶ More than half of the opioid prescriptions in the United States are written for patients with serious mental illness, who represent one-sixth of that population.¹¹ Maybe chronic opioid use for pain has more to do with vulnerability to opioids and less to do with a pain syndrome.

I now think about daily opioid use in much the same way as I think about daily prednisone use. Patients on daily prednisone have a characteristic set of medical risks from the prednisone itself, regardless of its indication. Yet we do not consider these patients addicted to prednisone. Opioid use may be similar.

Like most doctors, I am troubled by the

Total opioid use in acute pain was the best predictor of ongoing use, and chronicity began earlier than thought

continued rise in the opioid overdose rate.¹³ Yet addiction and death from overdose are not the only risks that patients on chronic opioids face; they also have higher rates of falls, cardiovascular death, pneumonia, death from chronic obstructive pulmonary disease, and motor vehicle crashes.^{14–17} Patients on chronic opioids for pain have greater mental health comorbidity and worse function.¹⁸

Most concerning, chronic opioid treatment for pain lacks proof of benefit. In fact, a recent study disproved the benefit of opioids for chronic pain compared with nonopioid options.¹⁹ When I meet with patients who are taking chronic opioids for pain, I often can't identify why the drugs were started or ought to be continued, and I anticipate a bad outcome. Yet the patient is afraid to stop the drug. For these reasons, chronic opioid use for pain strikes me as worth considering separately from opioid use disorder.

■ HOW THIS CHANGED MY PRACTICE

The studies described above have had a powerful effect on my clinical care as a hospitalist.

I now talk to all patients starting opioids about how hard it can be to stop. Some patients are defensive at first, believing this does not apply to them. But I politely continue.

People with depression and anxiety can have a harder time stopping opioids. Addiction is both a risk with ongoing opioid use and a possible outcome of acute opioid use.⁸ But one can struggle to stop opioids without being addicted or depressed. Even the healthiest person may wish to continue opioids past the point of benefit.

I am careful not to invalidate the patient's experience of pain. It is challenging for patients to find the balance between current discomfort and a possible future adverse effect. In these conversations, I imagine how I would want a loved one counseled on their pain control. This centers me as I choose my words and my tone.

I now monitor the total amount of opioid

I prescribe for acute pain in addition to the daily dose. I give my patients as few opioids as reasonable, and advise them to take the minimum dose required for tolerable comfort. I offer nonopioid options as the preferred choice, presenting them as effective and safe. I do this irrespective of the indication for opioids.

I limit opioids in all patients, not just those with comorbidities. I include in my shared decision-making process the risk of chronic opioid use when I prescribe opioids for acute pain, carefully distinguishing it from opioid use disorder. Instead of excess opioids, I give patients my office phone number to call in case they struggle. I rarely get calls. But I find patients would rather have access to a doctor than extra pills. And offering them my contact information lets me limit opioids while letting them know that I am committed to their comfort and health.

As an addiction medicine doctor, I consult on patients not taking their opioids as prescribed. Caring for these patients is intellectually and emotionally draining; they suffer daily, and the opioids they take provide a modicum of relief at a high cost. The publications I have discussed here provide insight into how a troubled relationship with opioids begins. I remind myself that these patients have an iatrogenic condition. Their behaviors that we label "aberrant" may reflect an adverse reaction to medications prescribed to them for acute pain.

Mary, my patient with postoperative pain after cholecystectomy, may over time develop opioid use disorder as Heather did. That progression may have begun with the hydrocodone I prescribed and the counseling I gave her, and it may proceed to chronic opioid use and then opioid use disorder.

I am looking closely at the care I give for acute pain in light of these innovative studies. But even more so, they have increased the compassion with which I care for patients like Heather, those harmed by prescribed opioids. ■

I now think about daily opioid use much the same way I think about daily prednisone use

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ADDRESS: Charles Reznikoff, MD, FACP, Department of Medicine, Hennepin County Medical Center, 701 Park Avenue, Minneapolis, MN 55415; charles.reznikoff@hcmcd.org