

## REVIEW

## Using opioid therapy for pain in clinically challenging situations: questions for clinicians

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## ABSTRACT

Healthcare professionals and organizations increasingly face the conundrum of treating patients with active substance use disorder, a history of personal or familial substance use disorder, or those at elevated risk for substance abuse. Such patients need compassionate care when facing painful conditions; in fact, denying them pain control makes it likely that they will seek out ways to self-medicate with illicit drugs. Yet it remains unclear how to safely and effectively treat patients in these challenging situations. The authors have formulated ten questions to address in order to provide adequate analgesia for such patients. These questions demand a highly individualized approach to analgesia. These ten questions involve understanding the painful condition (presumed trajectory, duration, type of pain), using validated metrics such as risk assessment tools, guidelines, protocols, and safeguards within the system, selection of the optimal analgesic product(s) or combination therapy, and never starting opioid therapy without clear treatment objectives and a definitive exit plan. It is tempting but inaccurate to label these individuals as “inappropriate patients,” rather they are high-risk individuals in very challenging clinical situations. The challenge is that both options — being in pain or being treated with opioids to control pain — expose the patient to a risk of rekindling an addiction. The question is how do we, as clinicians, adequately respond to these very perplexing clinical challenges?

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Increasingly, physicians are asked to manage moderate to severe pain in patients who are either active substance users or at elevated risk for opioid use disorder (OUD). This population can be particularly challenging to treat in that their need for adequate analgesia must be balanced against the risks of opioid exposure. One particular obstacle in finding analgesic solutions for this population is that it is a vast and not homogeneous population. Globally, 9.2 million people use heroin and an estimated 13.5 million take some form of legal or illegal opioids.<sup>1</sup> This does not include individuals who are in recovery. Thus, patients at all points on the spectrum

of opioid use, including those in recovery from substance use disorder plus those who may have other substance use disorders such as alcoholism or cocaine use, may present clinically with legitimate needs for pain control. These patients include people of all ages (including pediatric and geriatric patients), both sexes, all socioeconomic groups, and all educational levels. While there is a tendency to seek trends in OUD, for instance, that young Caucasian men are more likely to use opioids recreationally than older Asian women or that Americans are more likely to misuse opioids than Europeans, these are — at best — broad trends. Even the line between licit and illicit opi-

oid use becomes blurred as many patients have legitimate pain indications and valid medically supervised opioid prescriptions yet still “top off” with illicit street drugs. In some cases, patients previously treated with prescription opioid therapy may migrate to street drugs when they are unable to get refills for their pain medication. OUD is borne of diverse motivations that may include: experimentation, recreational use (“partying”), desire to experience psychoactive effects, curiosity, peer pressure, self-medication of emotional pain, and the casual or haphazard use for physical pain. There is a tendency in some healthcare settings now to avoid opioids entirely. However, not considering all of the tools in the toolkit may be unethical. In other words, denying prescription opioids to a patient in pain previously treated with chronic opioid therapy does not mean that patient will not take more opioids — it virtually assures that the patient will find and take opioids from some other source. When considering analgesic options for patients with a history of OUD or active substance use disorder, alternatives to opioid must be considered and exhausted first and opioids should only be used when absolutely necessary and then with safeguards, caution, and close supervision.

### A note on nomenclature

The terminology surrounding opioid use is evolving in an effort to be both more accurate and less stigmatizing.<sup>2</sup> To that end, the authors determined that it would be most accurate to describe the patients in our paper as patients in a “challenging situation” rather than as “challenging patients,” or addicted patients, or inappropriate patients. Patients facing moderate to severe pain are not “inappropriate” nor are their needs for pain management “inappropriate,” although they pose very real clinical challenges to the healthcare professionals who care for them. We also for the most part avoid the word addiction in favor of “opioid use disorder” (OUD).

### Methods

While this article reviews the relevant literature, it is neither a systematic nor a narrative review

but instead evaluates a clinical conundrum for many practicing clinicians: these are the questions we have asked ourselves in terms of how to manage pain in patients with substance use disorder or at high risk for substance use disorder. Clear-cut easy answers are not always available, in that analgesia must be individualized for the patient and pain patients — and even the subset of patients at elevated risk for substance use disorder are not a homogeneous group. The dilemma in terms of adequate analgesia in these challenging situations arises only after all other analgesic options have been explored and exhausted.

The authors of this paper formulated ten key questions which should be addressed in considering opioid analgesia for pain control in these patients and clinical experience, guidelines, and evidence-based literature was then used to help further explain these questions. These questions form the headings for the bulk of this article and involve: defining the pain and pain trajectory, using risk assessment tools, understanding system safeguards, determining the appropriate analgesic product(s), duration of therapy, endpoint of therapy with preplanned exit strategy, combination therapy options, and individualization of approach for the given patient.

### Results

Ten questions are important to address when considering using opioids or other analgesic products for patients in these challenging clinical situations. Table I presents a short summary of these questions with some key words and factors to consider.

#### What type of pain is involved and what is the pain trajectory?

Acute pain, such as traumatic pain or postoperative pain, can be mild to severe but typically has a well-described trajectory. Controlling acute pain as the body heals allows for at least an approximate pain control treatment schedule. This may be one of the most clear-cut types of pain to treat. Many types of acute painful conditions have the potential to become chronic pain, and chronic pain symptoms are more difficult to

TABLE I.—*A short summary of the questions to guide pain control therapy in challenging clinical situations.*

Key word	Question	Comments
Pain	What type of pain is involved and what is the pain trajectory?	Distinguish between acute pain and chronic pain as well as more complex types of pain, e.g. cancer pain.
Protocol	Is there a protocol in place for risk assessment?	Use the risk protocol of the hospital or clinic, if one is in place.
Guidelines	Are guidelines being used to formulate treatment strategies?	Numerous pain guidelines appear in the literature and should be used to craft the specific pain strategy.
Goals	Are there clear treatment objectives on which both patient and prescriber agree?	Functional goals are often more meaningful to patient than clinical assessments.
Safety Net	Are there built-in safeguards in the system?	In addition to using safety steps (such as urine assays), talk to patient and family about naloxone in the event of respiratory depression.
Optimal analgesic	What is the optimal analgesic for this patient?	Abuse-deterrent formulations of opioids may be appropriate, although there can be cost factors to consider.
Duration	How long is it presumed that opioid therapy will last?	Opioid therapy should never start without a clear endpoint; if opioid therapy must be prolonged, review frequently.
Cessation	What is the exit strategy?	Do not start opioid therapy without a clear exit point; with prolonged exposure, it may be necessary to taper opioids gradually to avoid withdrawal symptoms.
Combination	Would combination therapy be effective for this patient?	A small amount of opioid combined with acetaminophen or NSAIDs can be effective in relieving pain and result in lower net opioid consumption without sacrificing pain relief.
Individualization	Is pain control being adequately individualized for this particular patient?	Consider the patient's age, lifestyle, physical limitations, comorbid conditions, functional level, health/wellness goals, other concurrent pharmacological therapy, mental health, culture, and family life.

address as chronic pain is maladaptive, disconnected from the healing process, and likely involves aberrant neuronal signaling rather than physiological symptoms.<sup>3</sup> It is thought that appropriate treatment of acute pain might in some cases prevent the pain chronification process,<sup>4</sup> which is not fully elucidated.<sup>5</sup> Chronic postoperative pain (CPOP) has been estimated to occur at rates of 2% to 50%, depending on the type of surgery.<sup>6-9</sup> There are limited studies on CPOP in the literature and CPOP is a concern for all surgical patients.<sup>10</sup> Efforts are being made at identifying potential risk factors for surgical patients to develop CPOP, with acute postoperative pain emerging as a risk factor for CPOP.<sup>11</sup>

Cancer pain may involve pain from the underlying disease (such as tumors pressing against nerves) as well as pain associated with surgical procedures or chemotherapy. Cancer pain by nature is dynamic, changing with disease progression and remission, and is characterized by flares or paroxysmal breakthrough episodes of very severe pain against a background of continuous pain. Treating cancer pain requires an understanding of the disease, the patient's prognosis, current cancer treatments, and patient's

lifestyle. In the past decades, cancer has become an increasingly survivable disease with about two-thirds of cancer patients living at least five years with cancer, meaning that physicians now find themselves managing more and more patients with what could be termed "chronic cancer pain."<sup>12</sup> The old notion that cancer patients were somehow immune from OUD has been debunked,<sup>13</sup> but the burgeoning number of cancer patients living with "managed cancer" are associated with important clinical challenges. Of course, cancer patients at end of life and those experiencing severe pain symptoms may be aggressively treated in terms of pain control and patient comfort.

Chronic noncancer pain affects millions of people around the world, and the role of long-term opioid therapy in this population is controversial.<sup>14</sup> For one thing, opioids are not always helpful as long term therapy, in that they may result in negative changes over time in terms of how pain interferes with the patient's ability to work or participate in moderate activities compared to similar patients not taking opioids (odds ratios 9.2 and 3.7, respectively).<sup>15</sup> Often neglected in the discussion of opioid therapy today is

the fact that opioid-associated side effects can be treatment limiting and many patients dislike opioids.<sup>16</sup> A meta-analysis of 11 open-label extension studies (N.=2,445) found the majority of patients on long-term opioid therapy discontinued opioid before the open-label study concluded, but those who finished the study did achieve long-term and tolerable pain control.<sup>17</sup> In a study of shared-decision making between patients and prescribers, it was suggested that unless the net benefit of opioid therapy is significant pain reduction (defined as >2 points on a 10-point scale), the adverse effects outweigh the benefits.<sup>18</sup>

### Is there a protocol in place for risk assessment?

The risks for OUD are elevated in some patients and efforts have been made to objectively quantify these risk factors. The risk of OUD is constant but also dynamic, that is, it changes over time and with a variety of factors including disease progression, tolerance, lifestyle changes, mental health conditions, polypharmacy, comorbidities, and the patient's living situation.<sup>19</sup> Numerous risk factors for OUD have been identified in the literature including: higher pain intensity levels, mental health disorders, preadolescent sexual abuse, personal or familial history of substance use disorder, a history of legal problems, being a crime victim, drug cravings, younger age, and exhibition of classic drug-seeking behaviors, such as doctor shopping, frequently "losing" prescriptions, and demanding specific types of opioids.<sup>19</sup> Prolonged exposure to opioids is in itself a risk factor.

A variety of validated metrics are available for rapid, in-clinic assessment of risk factors, but their accuracy has been called into question.<sup>20</sup> These metrics include the Opioid Risk Tool (ORT), the Screener and Opioid Assessment for Patients with Pain, Version 1 tool (SOAPP-R), and the Brief Risk Interview.<sup>21-24</sup> The Centers for Disease Control and Prevention (CDC) maintain that the single most important risk factor in predicting OUD is a history of substance abuse.<sup>20</sup> Other risk factors — which may not be as prominent — include current use of benzodiazepines, use of antidepressants, male sex, unmarried status, non-Hispanic white race, taking higher doses of opioids, prolonged exposure to opioids, tobacco use, familial history of substance use dis-

order, lower socioeconomic status, and the use of angiotensin-converting enzyme (ACE) inhibitors. While "younger age" is often cited as a risk factor, there is no clear consensus on what that age range is (typically it ends around 30) and, furthermore, "older age" (sometimes defined as over 50, other times defined as over 65) has also emerged as a risk factor. Thus, age is probably not helpful as a real-world risk stratifier.<sup>25</sup>

### Are guidelines being used to formulate treatment strategies?

A study of opioid prescribing patterns found evidence of an opioid epidemic in the United States, Australia, and Canada but not in Germany, although all of these nations had guidelines in place regarding opioid prescribing. In these cases, all of the guidelines recommend regular re-assessment of long-term opioid therapy, but the German guidelines stated specifically that chronic opioid therapy was only appropriate for "responders," that is, those who could meet their treatment goals with tolerable adverse effects.<sup>26</sup> Response to opioid therapy may be an important and underutilized metric in many parts of the world where opioids are either deemed effective or ineffective.

The Treatment Improvement Protocol (TIP) 54 published by the Substance Abuse and Mental Health Services Administration specifically addressed how chronic pain may be managed in adults with or in recovery from substance use disorder and its guidance may offer insights into caring for these patients in other challenging clinical situations as well.<sup>27</sup> Patients at high risk for OUD in challenging clinical situations should unequivocally be referred to pain medicine experts or others with expertise at managing high-risk patients in pain, such as addiction specialists. The CDC issued guidelines for primary care physicians prescribing opioids in 2016, and recommended using opioids at the lowest effective doses for the shortest period of time possible.<sup>28</sup> While this guidance can be particularly helpful for patients with acute pain syndromes, it does not address painful conditions which may reasonably be suspected to last for months, years, or indefinitely. High-risk patients in challenging situations should be referred to a pain expert.



### Are there clear treatment objectives on which both patient and prescriber agree?

A shared decision-making process between patient and prescriber can be helpful in formulating a workable pain control plan. In acute care, the treatment goals are often obvious: to relieve pain long enough to allow for patient healing, with the understanding that pain treatment will cease as the patient recovers. For longer-term care, such as certain types of orthopedic surgery or chronic conditions, goals might be sufficient pain control to allow the patient to participate in rehabilitation therapy. The understanding in such cases may be pain control persists until the patient has had time to heal and regain function.

For cancer pain patients and patients with chronic pain, goals might be formulated more broadly and likely do not encompass a specific completion time. For example, goals might be functional (the ability to perform certain tasks of everyday life), improvements in sleep, and pain control. In some cases, long-term opioid therapy should encompass certain therapeutic goals, such as the ability to manage pain and achieve functional objectives without taking large amounts of opioids, for example, using combination analgesic therapy.

In all cases, it is important that the clinical team manage patient expectations and set realistic goals. Complete pain relief is almost never possible. The prescriber and patient should discuss how residual pain will be managed. Breakthrough pain can be particularly concerning for patients and if breakthrough episodes are a possibility, patients should be advised of its nature, likely duration, and possible ways to manage it. High-risk patients are typically better suited to structured dosing of medications and that should be disclosed to them early in therapy.

Patients should be informed and educated about nonpharmacological pain control measures, when they are reasonable alternatives, such as physical therapy, biofeedback, exercise, and lifestyle modifications. These measures may help with pain control and are beneficial in helping patients cope with their challenging situation. Active engagement in these aspects of care should be viewed as indicators of good faith on the part of the patient. Successful pain control in

challenging clinical cases requires the active engagement and participation of the patient as well as the clinician.

### Are there built-in safeguards in the system?

In challenging prescribing situations, clinicians must recognize that there is a risk that is inherent in the drugs, risk inherent in the patient, and risk inherent in the setting. The practice workflow at the clinic must be viewed objectively in terms of how well it can reduce the risk. A variety of safeguards have been identified which may be used to help monitor opioid use such as random pill counts, urine drug tests, the use of prescription drug monitoring programs (in many parts of the USA), and patient-prescriber treatment agreements.<sup>29, 30</sup> Prescribers must discuss these safeguards with patients prior to starting opioid therapy so that patients are aware of these measures and do not feel singled out when these measures are applied in the future. It is ideal if there is a relationship of mutual trust and confidence between patient and prescriber, but it is to be expected that not all patients with OUD will be forthcoming about their drug use.

Naloxone can be used to reverse opioid toxicity and is available in products intended for use by laypersons to rescue individuals who are suspected of having overdoses on opioids.<sup>31</sup> Many people with OUD and their families are not knowledgeable about naloxone,<sup>32</sup> so education for patient and family/caregivers is important. In many cases, opioid toxicity can be reversed with promptly administered naloxone. Naloxone, however, is a rescue medication, and does not prevent or treat OUD.

### What is the optimal analgesic for this patient?

The selection of the analgesic agent(s) is paramount in appropriate pain care, particularly for challenging patients. The prescriber must consider the pain mechanisms and prescribe the appropriate pain relievers, for example, opioids are effective in treating nociceptive pain but are not particularly effective in treating neuropathic pain, which may be better addressed with a gabapentinoid such as pregabalin or gabapentin. When considering multi-modal pain therapy for multimechanistic pain, it must be considered that no drug in

this situation is without risk. While NSAIDs and paracetamol may be effective pain relievers for some pain syndromes and are not drugs of abuse, they are associated with clinically established risks of morbidity and mortality. Other drugs, such as anticonvulsant adjuvant agents, may be associated with substance use disorder as well.<sup>33</sup>

Among opioid analgesics, there are some that are thought to be less likely to be abused. For patients with a history or active substance use disorder, it is beneficial to minimize their exposure to the potentially euphoric psychoactive effects of opioids if opioids are prescribed at all. Thus, opioids with minimal rewarding properties, such as tramadol, tapentadol, buprenorphine and codeine should be considered, if they are effective for the patient.<sup>27</sup>

Abuse-deterrent formulations (ADFs) of many opioid analgesics are available. ADFs are designed to reduce or deter misuse and abuse of the active agent. An ADF opioid can still be taken intact orally for nonmedical use, but the products are designed to make it very difficult to crush, dissolve, or draw the opioid into a syringe for injection. Other ADF products use combinations such that tampering with the product releases sequestered naltrexone that would blunt the psychoactive effects of the drugs.<sup>34</sup> ADF products have been advocated by the U.S. Food and Drug Administration (FDA),<sup>35,36</sup> although they remain controversial in that they are expensive, are often not reimbursed, and have been questioned in terms of the extent to which they actually work.<sup>37</sup> For instance, there is evidence that the introduction of an ADF product into a community results in a decrease in the inappropriate use of that particular opioid in that location,<sup>38,39</sup> but it is not clear whether the use of ADF products causes people with OUD to migrate to other opioids or if it leads to a net decrease in opioid misuse.

For pain patients in recovery for some form of substance use disorder, it may be helpful to initiate a conversation about opioid analgesics. For example, some patients in rehabilitation may be able to take opioids for a limited period of time under clinical supervision and may be able to self-monitor their use (“Am I taking this for pain control? Or am I using this drug for some other reason?”) Other patients may wish to discuss

pain control strategies with addiction specialists, psychological counselors, or other physicians. Prescribers should also consider how any possible opioid analgesics might interact with other drugs the patient is taking. For example, the CDC guidelines do not recommend the concomitant use of benzodiazepines and opioids,<sup>28</sup> which has been found to be associated with a higher risk for overdose morbidity and mortality.<sup>40</sup> Many opioids can have pharmacokinetic drug-drug interactions with other drugs, resulting in adverse effects.<sup>41-43</sup>

The duration of action (long-acting *versus* short-acting) of the opioid analgesic is important to consider. In a study of 319 unintentional opioid overdoses, it was found that patients taking long-acting opioids had a significantly elevated rate of overdose injury than patients taking short-acting opioids (hazard ratio [HR] 2.33, 95% confidence interval [CI], 1.26 to 4.32). This risk was greatest in the first two weeks of therapy (HR 5.25, 95% CI, 1.88 to 14.72).<sup>44</sup> Long-acting opioids are often preferred by those with OUD, as the pills contain a larger extractable amount of active ingredient than short-acting opioids.

#### How long is it presumed that opioid therapy will last?

The duration of expected opioid therapy can be a crucial question in finding the solution for pain control in people with substance use disorder. Clearly, a shorter and well-defined period of opioid use is preferable to more open-ended therapy duration; the risk for adverse effects likewise increases with prolonged exposure.<sup>45</sup>

Long-term use of opioids may start with an acute painful condition and an anticipated short course of opioid therapy, but the manner in which intended short-term opioid use might transition into chronic use have not been well documented.<sup>46</sup> The probability of long-term opioid use increases most in the first days of therapy (after five and 30 days of opioids) and then levels off after about 12 weeks of therapy. Patients at high risk for OUD in challenging situations should be closely monitored with the aim of terminating therapy as early as is both appropriate and possible. It may be helpful to discuss how long opioid therapy is to last, even if the exact duration is flexible (for example, three to five days

following surgery). Even if longer-term pain control is needed, opioid therapy should be frequently reviewed and not presented as a therapy of indeterminate duration.

### What is the exit strategy?

As stated earlier, setting analgesic goals should be part of shared decision-making with the patient. In some cases, the goal may be pain control to facilitate healing from trauma, rehabilitation following surgery efforts, function in terms of everyday activities with chronic painful conditions, or other specific objectives. Personalized pain goals, typically functional milestones, are often more clinically relevant to the patient than pain scores or other medical metrics. In a study of 347 pain patients, 80% of patients who were able to achieve their personal pain goals could discontinue analgesia and it is speculated that a personal goal may be a more accurate indicator of pain compared to a numeric pain intensity score alone.<sup>47</sup>

Opioid therapy should not be trialed without having an exit strategy in mind. There are a number of reasons to terminate opioid therapy: lack of efficacy, adverse events, intolerability, and harms to the patient. In some cases, opioid therapy may end when the pain has resolved or the patient has met treatment objectives. Patients should be advised that opioids cannot be stopped abruptly without risking the occurrence of withdrawal symptoms but that they can be discontinued under medical supervision with minimal risk and discomfort.

An exit strategy involves a systematic tapering of opioid over a period of time until the patient can stop taking opioids altogether with no or minimal withdrawal symptoms. Opioid tapering strategies have been described in the literature.<sup>48</sup> In general, the longer the duration of opioid therapy, the slower the tapering plan. Tapering should be discussed in plain language with the patient.

For a variety of reasons, patients with OUD may not be completely honest about their treatment goals, their level of pain or pain control, or their achievement of functional objectives, because they want to prolong opioid therapy. Regardless of their degree of risk for OUD, opioid patients today likely feel a sense of vulnerability about their access to pain control. Clinicians

should seek to establish an honest, trusting relationship with patients but also apply reasonable clinical judgment and exercise professional compassion when dealing with patients in pain.

### Would combination therapy be effective for this patient?

Multimechanistic pain is pain caused by more than one etiology, for instance, nociceptive pain with a neuropathic component or back pain with nociceptive pain, neuropathic pain, and muscle spasms. Combination therapy involves the use of multiple agents to treat pain, such as two or more analgesics with or without adjuvant agents, which may address each of the pain mechanisms. A good example of this is an antispasmodic, an opioid, and a gabapentinoid for the short-term pain control of severe lower back pain.

Combination therapy may also be initiated so that the patient consumes less opioids without sacrificing pain relief. For instance, opioid and nonopioid analgesics may be combined such that the patient takes less opioids but with pain relief equivalent to that of opioid monotherapy.<sup>49-51</sup> Many fixed-dose combination products (paracetamol plus oxycodone, paracetamol plus hydrocodone, paracetamol plus tramadol, paracetamol plus codeine) are commercially available or combination therapy can be delivered as two products (paracetamol or NSAID plus small amount of opioid) which allows for greater dosing flexibility. Other adjuvant agents (antidepressants, anticonvulsants, muscle relaxers) may be combined with reduced amounts of opioids for effective pain control. In some instances, it may be helpful to consider nonpharmacological treatment options that may be added to a drug regimen. Such nonpharmacological treatments might include: physical therapy, occupational therapy, massage, relaxation techniques, biofeedback, transcutaneous electrical stimulation, or meditation.

While combination therapy is generally recommended for a wide range of pain patients, it may offer high-risk patients in challenging situations special advantages. There is a paucity of randomized clinical trials on how to achieve effective pain control for high-risk patients in challenging situations, but it makes intuitive sense that limiting net opioid consumption by



TABLE II.—*Adjuvant agents that may be appropriate for pain therapy.*

Adjuvant agent	Mechanism/rationale	Product(s)/dose	Considerations
Gabapentinoids	Pain reliever, effective against neuropathic pain	Gabapentin (300-3600 mg/day); pregabalin (150 - 600 mg/day)	Side effects may be treatment limiting; abuse potential
Antidepressants	Analgesic effect occurs at doses lower than therapeutic dose for depression	Selective serotonin reuptake inhibitors (SSRIs), various products, fluoxetine, paroxetine, etc.	Products differ in dose, side effects
Muscle relaxants	Antispasmodics, reduces muscle spasticity and related pain	Carisoprodol among others (250-350 mg in four daily doses)	Short-term use only, maximum 2-3 weeks
NSAIDs	Anti-inflammatory effect, pain relief	Various. Ibuprofen (1200-3200 mg/d in divided doses), naproxen (250-500 mg day, in two doses), etc.	May be opioid sparing; fixed-dose combination products (NSAID + opioid available). NSAIDs have been associated with GI side effects and CV adverse events. Take at lowest effective dose for shortest amount of time
Acetaminophen (APAP)	Pain relief	Daily dose (all sources) limited to ≤4 g	May be opioid sparing; fixed-dose combination products (APAP + opioid available). Liver toxicity at supratherapeutic doses. May provide synergistic analgesia when used in combination with opioids

using combination therapy may be a prescribing consideration.<sup>52</sup> Combination approaches (opioid plus nonopioid) may allow for adequate analgesia in patients with high tolerance for opioids without resorting to supratherapeutic opioid doses (Table II).<sup>52</sup>

**Is pain control being adequately individualized for this particular patient?**

Individualized pain plans allow for detailed description of pharmacological regimen which is updated consistently based on patient response to analgesia. For instance, doses may be adjusted to achieve adequate analgesia, poorly tolerated drugs might be rotated to other agents, and routine pain evaluations and conversations with the patient might be used to modify therapy. Poorly tolerated opioids may be decreased in favor of combination therapy. Specific screenings may be beneficial for challenging patients, for example, drug monitoring programs have been recommended for chronic opioid patients who are scheduled for elective surgery.<sup>53</sup> Pharmacogenetics may offer interesting and important improvements in individualized pain care in the future, as genetic testing may help guide prescribers to optimal analgesia.<sup>54</sup> Other considerations in individualization of pain control include the patient's age (which may necessitate dose adjustments),

comorbidities, physical limitations (such as dysphagia), polypharmacy, lifestyle (housing, care), mental health, and culture.

**Conclusions**

All patients in pain can pose clinical challenges but for patients with active OUD, substance use disorder, or a history of substance use disorder, pain control poses special clinical challenges which must be navigated by pain specialists.

Pain can be challenging to manage for any patient but for patients with active substance use disorder or a history of substance use disorder, pain control is extremely challenging. Opioids must be low on the decision tree in the treatment of such patients, in that other pain management options should be explored and exhausted first. Nevertheless, there may be times when high-risk patients require opioid therapy. These clinical situations should be managed by pain specialists, possibly in consultation with other experts such as addiction medicine specialists. Pain must always be addressed, even in patients with active OUD. In fact, not treating pain in a person with OUD is no assurance that opioids will not be used — it likely means the opposite as such individuals may seek out illicit drugs to self-medicate uncontrolled pain. Pain experts can find ways

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to manage the challenging clinical cases where patients with OUD need opioid therapy. This requires individualization of care, good communication between patient and prescriber, and a thorough understanding of pain control regimens.

### Key messages

- More and more often, clinicians enter challenging clinical situations in which they must treat the pain of a patient at elevated risk for opioid use disorder or with active substance use disorder. There is no one-size-fits-all approach for this clinical scenario; instead, clinicians must approach each patient holistically and individually.
- The authors have formulated a series of questions that can help guide the decision-making process. These questions address the painful condition (duration, type of pain, trajectory), using guidelines and validated measures, taking advantage of built-in safeguards in the system, and, if opioids are required, the proper considerations for opioid therapy (appropriate product, dose, exit plan to terminate opioid therapy).
- Shared decision-making, such as mutually agreeable goals and strategies, can be helpful for patients willing and able to participate in their own therapy.
- Combination therapy, such as the use of acetaminophen or NSAIDs plus relatively small amounts of opioids, may be a good opioid-sparing strategy for many patients. Fixed-dose combination products are available commercially.

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