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Think twice: Evidence-based opioid sparing approaches to pain management

Physicians should exercise caution when prescribing opioids to treat pain given the current lack of effective tools for assessing a patient's risk of developing opioid use disorder.

ABSTRACT: Many British Columbians have become addicted to opioids as a result of unsafe opioid prescribing and the illicit opioid market. Although prescription opioid use disorder is associated with substantial morbidity and mortality, physicians currently have no way of identifying patients who can safely be prescribed long-term opioid therapy for chronic noncancer pain. A recent systematic review found that screening tools for identifying opioid-naive adult patients at risk of prescription opioid addiction were not particularly useful. Based on this review and a subsequent clinical article, we provide three clinical scenarios in which evidence-based recommendations can be made. While more research is needed, the risk posed by the rapidly evolving opioid overdose epidemic and the proliferation of illicitly manufactured fentanyl analogs warrant reducing the prescribing of opioids for opioid-naive individuals.

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An estimated 115 000 British Columbians have become addicted to opioids (oral communication, Bohdan Nosyk, BC Centre for Excellence in HIV/AIDS, 1 August 2018) as a result of unsafe opioid prescribing and the illicit opioid market. Canadian data on prescription opioid use are dated,[1,2] but recent US data suggest that more than one-third of US adults report prescription opioid use, with substantial numbers reporting misuse and disorders.[3] The BC Centre on Substance Use recently published a systematic review[4] that highlights the need for clinical strategies to reduce the number of new opioid prescriptions for chronic pain in an opioid-naive patient (defined as someone who has never been prescribed opioids or who is not currently taking opioids). The review indicates that the optimal strategy for preventing prescription opioid use disorder (OUD) in BC promotes safer opioid prescribing. A subsequent clinical article[5] provides some examples of how physicians in BC can help patients manage their pain.

A clinical case

A 31-year-old carpenter presents with persistent acute back pain after a fall at work 3 weeks earlier. An MRI of his spine has revealed no abnormalities. Despite the use of physiotherapy and nonsteroidal anti-inflammatories, he reports persistent excruciating pain, particularly when trying to work. He is growing increasingly anxious about not working and asks for low-dose opioid medication. He states that some of his co-workers have been able to return to work after injuries by using opioid medications for pain. His chart states that he has a history of excessive alcohol use but no longer drinks because of "problems in the past." He has no other psychiatric disorders or symptoms and is not taking any medications.

Is there a way to predict this patient's risk of developing OUD if he is prescribed opioids for his persistent acute back pain?

Risks of prescribing opioids

New evidence has raised questions about the benefits of using opioids to treat chronic pain[6,7] and shown how individuals who initially become addicted to prescription opioids may transition to using illicit opioids, including fentanyl.[8] In BC, rates of opioid prescribing and availability are strongly correlated with

rates of opioid overdose death.[9] More than 70% of men and nearly 50% of women in BC who have died of a prescription opioid overdose did not have an active prescription in the 60 days prior to their death.[10] This suggests that there is a significant diversion of prescription opioid medications in the province. More than 80% of people who use heroin say they started with prescription opioids.[11,12] Youth are often introduced to opioid use through diverted prescription opioid medications, which research has shown are incorrectly perceived as being safer than illegal street heroin.[13,14]

Risk assessment tools

Recent Canadian and BC guidelines require clinicians to reach a thorough understanding of a patient's risks prior to prescribing an opioid for pain.[15-17] Similarly, the Alberta Opioid Use Disorder Primary Care Pathway suggests that family physicians "consider [using the] Prescription Opioid Misuse Index (POMI) if [the] patient receives prescription opioids and OUD is suspected."[18] However, strategies used by clinicians to identify patients at high versus low risk of developing OUD have not yet been critically appraised.

To assess these strategies, the BC Centre on Substance Use conducted a systematic review of risk factors and risk prediction tools used to identify patients at risk of developing prescription OUD.[4] Of 1272 studies identified, four high-quality studies evaluating risk factors were analyzed.[19-22] They included 2 888 346 patients and 4470 cases that met the authors' definition of prescription OUD. Although the review identified 31 studies that evaluated risk prediction tools for prescription OUD, only two studies (which examined five tools in total) met the quality standards, and thus were included.[19,21] The review indicated that all available assessment tools for predicting risk of developing prescription OUD, including the most commonly used tools in BC—the Opioid Risk Tool[23] and the POMI,[24] are based on lower-quality studies or demonstrated extremely poor diagnostic performance when test performance was assessed. While a history of opioid or other substance use disorders, certain mental health disorders (e.g., personality disorder, somatoform disorder), and co-prescription of certain psychiatric medications (e.g., atypical antipsychotics) appeared useful, more studies are needed to validate those findings. Also, patients who were given a new prescription for an opioid with a supply for 30 days or more appeared to be at a greater risk of developing prescription OUD than patients who received a supply of opioids for less than 30 days.[22] When patients get to an opioid dose greater than 120 mg morphine equivalents per day, they have a higher risk of developing prescription OUD.[22] Conversely, only the absence of an affective disorder appeared modestly useful for identifying patients who had a lower risk of developing the disorder. No symptoms, signs, or risk factors were amenable to meta-analysis. The lack of high-quality studies suggests that physicians and nurse practitioners currently have no way of identifying patients who can safely be prescribed long-term opioid therapy for noncancer pain. These findings are supported by a growing body of evidence that medication discontinuation increases the risk of adverse opioid-related health care events among those who already receive opioid therapy for chronic pain.[25,26]

Long-term opioid therapy is unlikely to benefit most people with chronic noncancer pain.

Long-term opioid therapy

The body of literature on opioid-based pain therapy is revealing risks to long-term use of opioids. For instance, a 2015 systematic review sponsored by the National Institutes of Health reported a dose-dependent risk of serious harm from long-term opioid therapy,[27] including increased risk of overdose, OUD, fractures, myocardial infarction, and sexual dysfunction. The review also indicated there was insufficient evidence to determine the effectiveness of long-term opioid therapy for improving chronic pain and physical function. A subsequent meta-analysis of 96 randomized controlled trials involving more than 26 000 patients with chronic noncancer pain indicated that opioid medications provided little added value compared with non-opioid alternatives.[6] More specifically, while evidence from high-quality studies showed that opioid use was associated with statistically significant improvements in pain and physical functioning, the improvements were small and the risk of side effects was greater than the risk associated with placebos. Comparing the use of opioids with non-opioid medications showed a similar benefit for pain and physical functioning, but the evidence was from studies that were of low to moderate quality.

Evidence suggests that any benefit of opioid therapy for chronic pain may diminish within weeks.[6] Most opioid trials are limited to 6 weeks or less.[27] To address this, the 12-month Strategies for Prescribing Analgesics Comparative Effectiveness clinical trial with masked outcome assessment compared opioid and non-opioid medication therapy; it showed no additive benefit for using opioids. Opioids were not superior to non-opioid medications for patients with chronic back pain or hip or knee osteoarthritis pain.[7]

Three common clinical scenarios

Recent studies and our clinical experience in the BC opioid overdose epidemic suggest evidence-based recommendations can be made for three common clinical scenarios **[Figure, following page]**.

Patients with chronic pain who are not receiving opioid therapy: Opioid therapy should generally be avoided in opioid-naive patients without cancer or palliative care needs given the limited likelihood of benefit and the considerable evidence of opioid-related harm.[27] Further, clinicians who hope to use the clinical examination to screen for high-risk patients or identify patients able to take opioid analgesics safely should be aware there are no symptoms, signs, or screening tools that appear to be particularly useful, and commonly used screening instruments provide no diagnostic value.[4] Our patient, the carpenter, presented to a physician with persistent pain and anxiety despite several weeks of non-opioid therapy. Overall, the incidence of OUD in the context of pain care is estimated to be 2.8% (range 0.10% to 34.0%).[4] Based on

this incidence rate and the results from the earlier systematic review,[4] none of the carpenter's symptoms or signs are particularly helpful for determining the likelihood of developing prescription OUD, except for his history of alcohol use. A diagnosis of mild alcohol use disorder could be pertinent, for a positive likelihood ratio (LR) range of 6.1 to 17.0, which indicates that if opioids were prescribed he might be at higher risk of developing disordered use (approximately 14.9% to 32.9%). However, since he does not have a psychiatric history and is not on psychiatric medications (positive LR range 2.2 to 5.8), his risk of developing OUD may be somewhat limited (6.0% to 14.3%). Given the extremely broad range of estimates of risk, as well as the limited ability of screening tools to discern high-risk from low-risk patients, it would be at the clinician's discretion whether a trial of opioid-based therapy would be appropriate. Recent literature has suggested there are limited benefits of opioid-based therapy, so this must be balanced against the risks of OUD and other harm, including overdose.[7]

Patients with chronic pain who are receiving opioid therapy: An approach involving individualized care must be employed for patients already using opioids.[27] While the literature suggests that there is potential for improved pain relief and physical functioning with slow opioid withdrawal, new trials are needed to best guide this approach.[28] A decision to withhold opioid therapies must be balanced against the serious risks of exacerbating pain, contributing to opioid withdrawal syndrome, encouraging a transition to street opioid use, and other harms.[25] For instance, a recent study of Medicaid beneficiaries in Vermont who filled daily high-dose opioid prescriptions for at least 90 consecutive days and subsequently discontinued these prescriptions showed that 49% of the beneficiaries had an opioid-related adverse event, defined as a hospitalization or an emergency department visit with a primary or secondary diagnosis of opioid poisoning or substance use disorder.[25] At the same time, given the prevalence of and the risks associated with prescription opioid diversion and misuse,[3] the use of opioid agonist therapy should be increasingly considered when OUD emerges (e.g., a problematic pattern of opioid use leading to clinically significant impairment or distress). Support for this approach is provided by the proven benefits of opioid agonist therapy in the prescription OUD context and evidence that buprenorphine/naloxone may provide analgesia similar to that of full opioid agonists. This approach will require that efforts be redoubled to overcome barriers to opioid agonist therapy, including improving access to OUD care in primary care.[29]

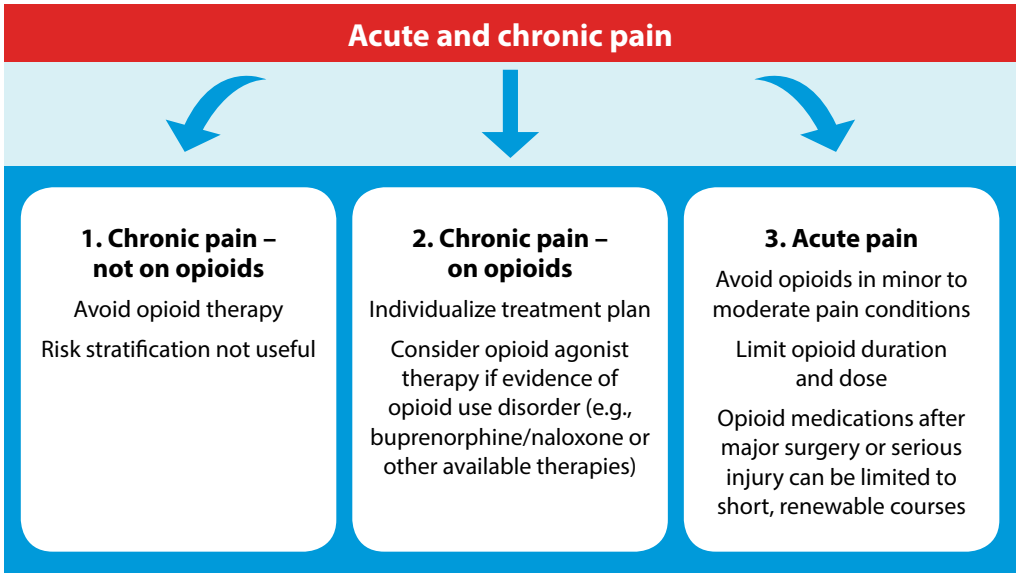

FIGURE. Evidence-based opioid sparing pain management strategy. *Source: Adapted from Wood and colleagues.*[5]

Patients with acute pain: Non-opioid therapy should be favored in those patients with minor to moderate acute pain. This is recommended because most chronic pain initially presents as minor to moderate acute pain, the benefits of opioid therapy may diminish rather quickly, and prolonged prescription opioid use increases the risk of developing prescription OUD. While there are benefits to opioid use for severe acute pain, it is important that the dose and duration be limited to short (e.g., less than 1 week), renewable (if necessary) courses.

Finally, physicians urgently need to be educated about both the risks of opioid-based therapy and the lack of benefits in many cases. In an effort to reduce inappropriate opioid prescriptions for opioid-naive patients in the province, the Therapeutics Initiative has collaborated with the BC Centre on Substance Use on a tool that provides prescribing portraits to physicians (www.ti.ubc.ca/portrait).[30]

Conclusions

While more research is still needed, recent studies and clinical experience suggest that reducing opioid prescribing for opioid-naive individuals is critical for improving public health and safety. There is currently no way to identify patients who can safely be prescribed long-term opioid therapy for noncancer pain. Physicians need to think twice, exercise caution, and generally avoid making assumptions about a patient's risk of developing prescription opioid use disorder. ■

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Competing interests

None declared.

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There is no valid tool or valid way to identify patients at low risk for opioid use disorder when starting opioids.

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