

Using of opioids for chronic pain: Controversies, guidelines, research needs

First in a series of five articles, Norm Buckley and Jason Busse explore the trials and tribulations associated with using opioids for chronic pain, particularly in Canada

The prescription of opioids for chronic pain is both clinically controversial and a highly politicized arena. Although rigorously developed clinical practice guidelines, when followed, can improve patient care, a number of other issues affect the behaviour of physicians, other healthcare providers and agencies responsible for access to treatment. This is the first of five editorials that will be published over the next year that will review the use of opioids for chronic noncancer pain, with a particular focus on Canada.

Clinical controversies and opioid prescriptions

The clinical controversy arises due to the absence of clinical trials that enroll complex patients that attend for care in practice and limited follow-up among randomized trials in what is by definition a long-term condition. A significant proportion of patients experiencing chronic pain also have other medical or mental health disorders and are receiving disability benefits or involved in litigation. Such patients are typically excluded from clinical trials, likely as they are anticipated to have a worse prognosis. This may help address the needs of an industry sponsor to achieve positive results, but the generalizability of findings to more complex patients is uncertain.

Randomized trials of opioids also do not follow patients long enough to identify issues that may arise during extended treatment. This is relevant to a condition such as chronic pain, which is typically non-resolving. Trials address short-term benefits and harms and are not conducted over more than 6 or rarely 12 months.

The importance of trustworthy and thorough guidelines

Trustworthy guidelines require high- quality, relevant research to inform them or become guidelines based on expert opinion. In the current guideline practice using decision-making conventions such as GRADE, a strong recommendation is expected to represent a decision that virtually all patients would agree with based on the clinical evidence and patients' values and preferences. In the 2017 revision of the Canadian Opioid Guideline, the panel was able to make 10 recommendations out of 24 topics that had been identified as important. Only four of ten were sufficiently supported by clinical trial evidence to be considered 'strong' recommendations. This is obviously not an optimal situation, so it speaks to the need to support large-scale, long-duration clinical trials that recruit widely varying groups of patients with complexities representing the range of conditions

experienced by people living with pain. Another option is to optimize use of registry data and long term follow up of clinical cohorts that would inform events associated with opioids for chronic noncancer pain that are either infrequent or require a long time to manifest. This may become more feasible now that the International Classification of Diseases version 11 will include chronic pain as a diagnosis, thus making it a searchable item in administrative health databases.

The politics of opioids and chronic pain

The politically charged arena is a function of several factors. One of them is the status of chronic pain as an ‘invisible disease’- while injury, tissue damage and trauma may be clearly quantifiable, the experience of pain is uniquely determined in each patient, leading to our consideration of chronic pain as a ‘bio-psycho-social’ phenomenon. The second is the diversion of prescribed opioids into uses considered ‘illicit, recreational or misuse’, making a link at least to some eyes between prescription opioids and illicit opioids- i.e., drug trafficking. The nature of pain as an invisible disease makes it easy to be skeptical about the ‘real’ need for analgesics amongst people living with chronic pain.

A focus on the use of opioids arises out of physicians’ desire to address pain using a medical model of thinking about chronic pain, with few effective pharmacological tools, and a marketing approach that has been described as high pressure. In fact, in the United States the marketing strategies have led to prosecution of pharma companies for the contributions of their products to what is described as an opioid crisis. This crisis is characterized by an ever-increasing number of deaths associated with prescription opioids in the years 2005-2015, and subsequent to that with a dramatic increase in deaths from high potency illicit products that sometimes replaced prescription opioids when prescribing was curtailed.

Canadian guidelines for the systematic use of opioids for chronic pain

Curtailing of prescribing came through several pathways, including guideline recommendations, the lay press, and the behaviour of some medical regulators in pursuing physicians prescribing opioids for chronic pain. In Canada and the United States guidelines were created to bring a systematic approach to the use of opioids. Canadian Guidelines appeared in 2010, and were revised in 2017, with a third revision underway at the present time. Guidelines in the US came from the American Pain Society in 2009, the Centres for Disease Control in 2016, with a revision released in 2022, and the US Department of Veterans’ Affairs in 2017, also with a revision released in 2022. The CDC and VA guidelines carried a strong philosophical opposition to use of opioids for chronic pain, while rejecting consideration of published evidence as the follow up periods in published trials were deemed too short to be relevant to the chronic nature of the pain conditions addressed.

While the Canadian guidelines suggested approaching patients already prescribed high-dose opioids ($\geq 90\text{mg}$ morphine equivalent/day) for ‘tapering to the lowest effective dose’, tapering was identified as not always being possible and it could be paused if pain or

function worsened on the lower dose. The 2016 CDC guideline was strongly in favour of tapering to a low dose. In Canada one provincial regulator strongly supported tapering, to the point of mandating this as a standard of care at one point, while another provincial regulator actively pursued the sanctioning of physicians prescribing high doses of opioids. The public press also reported comments by individual opinion leaders about the need to reduce opioid prescribing. The net effect of this was that in some cases patients whose opioid analgesics were withdrawn sought replacement with illicit opioids. Illicit opioids of very high potency have become the largest source of deaths due to overdose.

Preparing for the future examination of opioids for chronic pain

Over the next four editorials we will consider current evidence about the use of opioids for chronic pain, the extent and impact of the ‘opioid crisis’ in Canada, changes in prescribing and the role of prescription versus illicit opioids in the crisis of overdose related deaths, and finally the federal government’s activities over the past 15 years in addressing the opioid crisis in Canada.

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