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Framing of the opioid problem in cancer pain management in Canada

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ABSTRACT

Two guidelines about opioid use in chronic pain management were published in 2017: the *Canadian Guideline for Opioids for Chronic Non-Cancer Pain* and the European Pain Federation position paper on appropriate opioid use in chronic pain management. Though the target populations for the guidelines are the same, their recommendations differ depending on their purpose. The intent of the Canadian guideline is to reduce the incidence of serious adverse effects. Its goal was therefore to set limits on the use of opioids. In contrast, the European Pain Federation position paper is meant to promote safe and appropriate opioid use for chronic pain.

The content of the two guidelines could have unintentional consequences on other populations that receive opioid therapy for symptom management, such as patients with cancer. In this article, we present expert opinion about those chronic pain management guidelines and their impact on patients with cancer diagnoses, especially those with histories of substance use disorder and psychiatric conditions. Though some principles of chronic pain management can be extrapolated, we recommend that guidelines for cancer pain management should be developed using empirical data primarily from patients with cancer who are receiving opioid therapy.

Key Words Chronic pain, cancer pain, pain, opioids, Canadian pain guideline (2017), European pain guideline (2017), mental health, substance use disorders

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INTRODUCTION

The World Health Organization has described opioids as essential medicines for pain control. However, there are multiple barriers to opioid use that prevent health care providers from using opioids to their full potential for adequate pain control[1]. Opioid distribution shows substantial inequity, with 17% of the world's population consuming 92% of the world's supply[2]. In 2009, the proportions of the total global morphine supply consumed by the United States, Europe, and Canada were 56%, 28%, and 6% respectively[3]. Even in countries with access to prescription opioids, pain is inadequately treated, with one third of patients with cancer experiencing chronic pain[3,4]. Barriers to opioid use by primary care physicians (PCPs) include insufficient knowledge, fear of dependence, diversion, and regulatory scrutiny[2]. Efforts are therefore focused on limiting opioid use[5].

Since the start of the 2000s, opioid prescriptions have increased, with a parallel increase in addiction and the prevalence of aberrant opioid-taking behaviours[6,7]. In 2016, North American authorities declared public health crises because of the epidemic-like overdose deaths from prescription, diverted, and illicit opioids[8,9]. In response, the Michael G. DeGroote National Pain Centre at McMaster University collaborated with Health Canada to develop the 2017 *Canadian Guideline for Opioids for Chronic Non-Cancer Pain*[5], herein called the 2017 CG. Although it has been explicitly stated that the guideline does not address opioid use for acute pain[5], patients with cancer or in palliative care or those with substance-use disorders (SUD) could inadvertently be affected by the recommendations.

Opioids are important for cancer pain treatment and the 2017 CG might influence how opioids are prescribed to cancer patients[10]. Cancer pain is prevalent in 39% of patients after treatment, in 55% during treatment, and in 66% with metastatic disease[11]. Almost 38% of patients with metastatic disease report moderate to severe pain, and almost 33% are undertreated for their pain[11,12]. Another review stated that 51% of all cancer patients experience pain regardless of cancer type and stage, but that up to 66% of patients with metastatic disease experience pain[13]. Canadian research indicates that opioid prescription declined by 12% in Ontario between 2010 and 2013, and

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by 2% across Canada between 2013 and 2015[6,7]. However, opioid-related hospital visits increased by 13%, and the rate of drug abuse remained the same[6,7].

Opioid use and its associated harms are significantly less frequent in Europe than in North America[14]. In 2017, the European Pain Federation (EPF) released a position paper to promote opioid use for chronic pain management[15]. The EPF convened to address poorly managed pain, rather than opioid-related harms[15]. The EPF provides expert consensus recommendations for PCPs and other non-specialist health care professionals about safe opioid use[15].

The purpose of this article is to compare the Canadian guideline with the EPF guideline for opioid use in chronic pain to demonstrate how different research questions concerning a similar topic can lead to different outcomes. Each guideline elected to focus on a different aspect of opioids: The EPF guideline focuses on the public health concern of poorly managed chronic pain; the Canadian guideline is primarily concerned with reducing opioid-related harms.

Guideline Development and Format

The EPF developed its guideline by summarizing the evidence. If data were lacking, European physicians and scientists provided recommendations[15]. Details about the development of the paper were not published, nor were patients involved[15]. A flow chart is used as a stepwise guide to opioid initiation and treatment of opioid-related adverse effects[15].

To develop the 2017 CG, Busse *et al.*[16] examined available evidence using the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) system. The guideline panel consisted of 13 clinicians and 2 patient representatives. Clinicians with diverse opinions about opioid use for chronic pain participated in advisory roles in the associated clinical expert committee, and 16 patients with chronic pain formed the patient advisory committee[5,16]. The 2017 CG is a revision of the 2010 *Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain*[17]. The 2010 guideline was difficult to implement because of suboptimal formatting and excessive length[18]. The 2017 CG therefore uses concise statements to guide clinical assessments. The sections focus on detailed recommendations, practical information, strength of evidence, preferences and values, resources, and other considerations. The authors partnered with Making GRADE the Irresistible Choice to provide the guideline online.

Opioid Therapy Initiation

Both guidelines affirm that non-opioid therapy should be implemented and exhausted before opioids are started[15]. Based on the quality of the evidence and proven efficacy, the 2017 CG specifies the eligible patient populations and whether individuals in those populations should be considered for opioids[5]. It recommends controlled-release opioids for continuous pain and fast-acting formulas for activity-related pain[5]. The EPF guideline requires a comprehensive evaluation of the patient to determine whether opioid therapy is suitable[15]. Patients discuss and document treatment goals with their PCP, and they receive education about the benefits and risks of opioids and about appropriate use and storage. The EPF recommends controlled-release opioids to enhance compliance, reduce breakthrough pain, and decrease the likelihood of addiction[15].

Opioid Switching and Maintenance

Both guidelines state that patients receiving opioid therapy should be monitored to ensure that treatment remains beneficial and necessary[19]. Both guidelines recommend starting at the lowest dose, with a supervised trial period[19]. The 2017 CG suggests to start at a dose less than a 50 mg morphine-equivalent daily dose (MEDD) and to maintain the dose at less than 90 mg MEDD. Involving pain specialists if a patient requires a higher opioid dose is encouraged[19]. The EPF recommends seeking expert opinion at doses more than 120 mg MEDD[19].

However, consensus about equianalgesic MEDD opioid conversion ratios is lacking. Recommendations with specific dose cut-offs might not be appropriate given the individual response to opioids[19]. Although the risk of overdose or SUD increases as the daily dose rises, there is no clear threshold dose; respiratory distress can occur at less than 20 mg MEDD[20,21]. For patients switching between opioids, both guidelines suggest calculating the MEDD of the new drug and reducing the dose by 25%–50%[5,15]. Alternatively, PCPs can lower the original opioid dose while gradually increasing the new opioid dose[5,15]. The daily dose of one opioid does not necessarily exert the same effects as the daily dose of another opioid[19]. Both guidelines recommend considering patient-specific attributes such as organ function, drug tolerance, age, and body surface area when prescribing opioids[19].

Both guidelines recommend tapering and discontinuing opioids for patients not meeting treatment goals or those demonstrating signs of misuse[5,15]. The timing for tapering opioid therapy differs between the guidelines. The 2017 CG recommends tapering for anyone receiving more than 90 mg MEDD[5]. The EPF guideline recommends tapering after 6 months, followed by a "drug holiday" to determine whether opioid therapy is required[15]. The focus on dose alone could propagate a fear of regulatory sanctions and encourage negative attitudes toward patients who require higher doses.

Cancer Pain Management

Cancer survivors can continue to experience physiologically complex pain years after cessation of chemotherapy[22,23]. The prevalence of chronic pain in survivors ranges from 16% to 50%; care for those patients is often transferred back to PCPs[24,25]. The PCPs might be more reluctant than specialists to prescribe opioids, likely because of a lack of training, potentially making cancer survivors vulnerable to the effect of the new guideline[24]. Almost one third of PCPs report delaying opioid prescriptions for patients with cancer until the terminal phase of disease or unbearable pain[24]. A pan-European survey about chronic pain management revealed that 84% of PCPs perceived their training in pain management to be inadequate[26]. Others, citing lack of supportive resources, reported allocating insufficient time to assess and monitor patients[27–29]. The World Health Organization guideline for cancer pain management proposes opioids for severe pain[21], and yet systematic reviews of the quality of cancer pain management in Europe, North

America, Asia, Africa, and Australia found that one third of patients do not receive pain medication proportional to their pain intensity[4,10,24,30]. In addition, 37% of PCPs cited fear of regulatory review as a reason to avoid prescribing opioids, and some admitted to reducing opioid doses to avoid investigation[31]. Furthermore, patients taking chronic opioids have reported stigmatization[32,33]. An estimated 34%–86% of health care professionals overestimated addiction or tolerance likelihood[24,34]. In another study, 28% of PCPs believed that any patient given opioids is at an increased risk for addiction[35].

The inevitability of pain for cancer patients is known[36]. Patients with painful bone metastases are often under-medicated[36]. Opioids can be used at all stages of bone metastases[36]. Considering that cost and access to opioids are not a limitation for Canadian palliative care physicians and oncologists, pain management guidelines play a significant role in the under-prescription of opioids to patients with metastatic disease[36]. Increasing physician and patient education about opioid use can improve pain management in cancer patients[36].

Some patients might require opioids alone or in combination with other substances for continuous drug delivery to achieve appropriate analgesia[13]. Multidisciplinary symptom management is therefore required to achieve adequate pain control for patients with metastatic disease[13]. Implementing pain management strategies from the early stages of cancer to metastatic disease—before the pain is unbearable—would be beneficial[13]. Canadian recommendations for breakthrough cancer pain state that 5%–20% of the total daily opioid dose can be used to treat breakthrough cancer pain and that using a "two-formulations" approach to target different mechanisms of action can improve pain control[37]. Patients receiving opioids should be closely monitored, but addiction concerns should not prevent physicians from prescribing opioids[37]. The 2017 CG could hinder receipt of appropriate pain management for those patients and thus further compromise their quality of life.

Mental health disorders, including depression and anxiety, are prevalent in 50% of patients with chronic pain and in 29%–38% of patients with cancer[38]. The association between psychiatric conditions and pain is well-established; the treatment of such conditions could improve pain control, and the psychiatric illness might improve because of adequate pain management[39]. The EPF guideline does not comment on the issue of concurrent mental health and opioid prescription. The 2017 CG advises postponing opioid therapy until psychiatric disorders are stable[5]. Exclusion of patients with such disorders from opioid therapy for chronic pain management could negatively affect their quality of life and damage the physician–patient relationship[39].

Neither guideline addresses obstacles to opioid prescription and pain management in susceptible populations. Patients with SUD often require higher doses of opioids, and yet they are prescribed lower doses than patients without SUD[40]. Attitudes, beliefs, knowledge, and fear of regulatory sanctions on the part of PCPs can prevent access to opioids in people with SUD and psychiatric conditions[41]. The EPF guideline states that opioids should be considered in patients with chronic pain regardless of underlying comorbidities, and referral to a specialist is recommended for those at increased risk for SUD[15]. The 2017 CG suggests that patients with SUD be jointly treated by pain and addictions specialists[5]. However, there is a strong recommendation to exclude those patients from opioid therapy, even if non-opioid therapy has been used and proved to be ineffective[5].

SUMMARY

Addressing the underlying sources of pain is important for effective pain management. Patients with cancer can experience the serious harms associated with opioid addiction and misuse just as patients with chronic non-cancer pain can. We do not intend to suggest that opioids are appropriate for all cancer patients; rather, we recommend an evidence-based, open-minded strategy for opioid use in pain management. Neither the Canadian nor the EPF guideline is ideal for cancer pain. The dose cut-offs in the 2017 CG could lead PCPs to follow them as "rules" rather than recommendations and could result in fear of opioids and increased regulatory scrutiny, hindering access to pain control in vulnerable populations. The Canadian guideline might result in negative outcomes, such as undertreatment, stigmatization of patients, and damage to the physician–patient relationship, especially for cancer patients with psychiatric disorders and SUD. The EPF guideline is less restrictive, but could be confusing for providers inexperienced in cancer pain management. Safe and appropriate opioid use should be promoted for all patients and not just for those with addiction. Given all the foregoing considerations, we recommended that an update to the guidelines for cancer pain management be undertaken.

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CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and we declare that we have none.

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