## COMMENTARY

## Addressing the limitations of the CDC guideline for prescribing opioids for chronic noncancer pain

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Competing interests: All of the authors are members of the guideline development group for the Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain. David Juurlink was a member of the Stakeholder Review Group for the CDC Guideline for Prescribing Opioids for Chronic Pain. No other competing interests were declared.

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The excessive use of opioids for chronic noncancer pain represents a serious public health problem in Canada, and health care regulators face considerable pressure to adopt stricter policies to curb prescribing practices. In March 2016, the United States Centers for Disease Control and Prevention (CDC) issued a guideline for prescribing of opioids for chronic pain.1 Because it raises many cautions regarding opioid prescribing, and if followed would undoubtedly reduce opioid prescribing and related harms in Canada, many regulators and commentators have welcomed the guideline. However, it does have important limitations.

The limitations of the CDC guideline include largely restricting involvement to experts who have been critical of opioid use for chronic noncancer pain,<sup>2</sup> limited involvement of patients, excessive restrictions on selection of evidence (e.g., insisting on studies with a follow-up of one year or more excluded more than 100 randomized controlled trials (RCTs) of treatment with opioids in shorter durations); suboptimal application of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) rating system to address evidence quality;<sup>3</sup> excessive use of strong recommendations in the face of lowquality evidence; and vagueness in some recommendations.

Examples of this last limitation include guidance for clinicians to "consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient," and to "continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety."1 These recommendations represent good practice, but what clinicians require is succinct, specific guidance on how to make such decisions.

The CDC provides a strong recommendation to avoid increasing the dosage of opioids to 90 morphine milligram equivalents (MMEs) or more per day for patients with chronic noncancer pain.1 In a major omission, the guideline fails to address clearly how clinicians should manage patients currently prescribed dosages that are in excess of 90 MME per day. A large number of patients with chronic noncancer pain in Canada are prescribed opioids in dosages over this threshold: for example, a 2013 cross-sectional study involving 260 adult patients attending a tertiary care chronic pain clinic in Ontario found the median opioid dosage was 180 MME per day (interquartile range 60–501 MME per day).4

Overly aggressive adoption of the CDC guideline may lead to harm if physicians try to abruptly transition patients already receiving opioids at high doses to much lower doses. Harms could include withdrawal reactions, uncontrolled pain, anxiety for patients and loss of trust in their physicians. Such consequences could leave patients desperate.5 There is already preliminary evidence that in British Columbia, where the CDC guideline recommendations have been adopted as standards of practice,6 some patients have sought illicit opioids in the wake of reduced prescribing by physicians.<sup>7</sup> With the profusion of counterfeit fentanyl in Western Canada, the consequences could be fatal.8

Our group is updating the 2010 Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain. Our guideline development process will incorporate the strengths of the CDC guideline and address its deficiencies. We have determined the focus for our recommendations through in-depth consultation with patients, clinicians, researchers and regulators, engaging key representatives from all sides of the debate.

We are using the systematic review and guideline methodology developed by the GRADE working group<sup>3</sup> and the Institute of Medicine,<sup>9</sup>

## KEY POINTS

- Some Canadian regulatory bodies have endorsed the Centers for Disease Control and Prevention (CDC) Guideline for Prescribing Opioids for Chronic Pain despite its important limitations.
- A major omission is the CDC guideline's failure to address clearly how clinicians should manage patients currently prescribed doses in excess of 90 morphine milligram equivalents per day.
- The forthcoming Canadian opioid guideline will incorporate the strengths of the CDC guideline and address its deficiencies.

and the implementation model developed by the ninth iteration of the American College of Chest Physicians antithrombotic guideline. <sup>10</sup> Our approach will use recent methodologic advances to improve evidence syntheses, guide subgroup analyses, manage conflicts of interest and optimize presentation of data to facilitate interpretation. A draft of our final guideline recommendations will be available for external review in the first quarter of 2017.

It is likely that we will find limited evidence to inform some of our recommendations, particularly in the area of tapering, weaning or opioid rotation. We have formed a subcommittee comprising clinicians with expertise in these areas, whose experience will supplement the evidence. Randomized controlled trials involving opioid treatment for chronic noncancer pain typically report limited follow-up. We will consider all trials that follow patients for one month or more and perform meta-regression analysis to explore whether treatment effects are influenced by duration of follow-up.

We also anticipate challenges in synthesizing the evidence for effectiveness of opioids, because most RCTs report continuous outcomes for pain, function and quality of life — often using different outcome measures. The Cochrane Collaboration (http://handbook.Cochrane.org/) recommends pooling different measures that tap into a common domain (e.g., pain) by converting to a standardized mean difference (SMD). However, this measure of effect is difficult to interpret and influenced by differences in heterogeneity among study populations: when the true underlying effect is the same, studies with greater heterogeneity in pain scores at baseline will nevertheless result in a smaller SMD than studies enrolling patients with more homogeneous scores. We will convert all continuous measures for each domain to a single instrument and use the established minimally important difference (MID) to calculate the probability of experiencing a treatment effect greater than the MID.<sup>11</sup>

We anticipate these guidelines will help address deficiencies in pain education in medical schools in Canada. We have partnered with the Making GRADE the Irresistible Choice (MAGIC; available at www.magicproject.org) initiative to provide the updated guideline in digitally structured, multilayered presentation formats online and offline, including decision aids to facilitate use of guideline recommendations for decision-making in shared care. MAGIC also facilitates integration of guideline recommendations into electronic medical records as decision support systems.

The CDC guideline provides useful initial guidance but has important limitations. Our recom-

mendations will provide further guidance for frontline clinicians in efforts to reduce opioid prescribing while meeting the needs of all patients with chronic noncancer pain, including those currently using high-dose opioids.

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