Jan. 30, 2017

Draft Recommendations & Rationales for the 2017 Canadian Opioid Guideline

1. When considering first-line therapy for patients with chronic non-cancer pain, we recommend optimization of non-opioid pharmacotherapy and non-pharmacological therapy, rather than a trial of opioids (**Strong recommendation, Low quality evidence**).*

Rationale: Opioids, when added to non-opioids achieve, on average, modest improvements in pain and function at the cost of very frequent physical dependence, frequent addiction, and rare non-fatal unintentional overdose and death. A variety of non-opioid therapies as first-line treatment for patients with chronic non-cancer pain achieve a similar magnitude of improvement in pain and function but without the problems of dependence, addiction, and non-fatal overdose.

2. For patients with chronic non-cancer pain, without current or past substance use disorder and without other current serious psychiatric disorders who still experience persistent problematic pain despite optimized non-opioid therapy, we suggest a trial of opioids rather than continued non-opioid therapy. (**Weak recommendation, Moderate quality evidence**).

> Remark: By a trial of opioids, we mean initiation, titration, and diligent monitoring of response, with discontinuation of opioids if important improvement in pain or function is not achieved.

Rationale: Opioids, when added to non-opioids achieve, on average, modest improvements in pain and function. Adverse effects include relatively frequent constipation, nausea and vomiting, cognitive changes, dependence, and addiction, and rare death and non-fatal unintentional overdose.

3. For patients with chronic non-cancer pain with an active substance use disorder we recommend against the use of opioids (**Strong recommendation, Low quality evidence**).*

> Remark: Clinicians should, if not yet addressed, facilitate treatment of the underlying substance use disorders.

Rationale: Low quality evidence suggests a possible substantial increase in the very serious adverse outcomes of unintentional non-fatal overdose and death in patients with active substance abuse disorder using opioids.

4. For patients with chronic non-cancer pain with a current serious psychiatric disorder whose non-opioid therapy has been optimized, and who still experience persistent problematic pain, we suggest stabilization of the psychiatric disorder before considering a trial of opioids (**Weak recommendation, Low quality evidence).**

Rationale: Low quality evidence suggests a possible large increase in the very serious adverse outcomes of unintentional non-fatal overdose and death in patients with serious psychiatric disorder using opioids.

5. For patients with chronic non-cancer pain with a history of substance use disorder, whose non-opioid therapy has been optimized, and who still experience persistent problematic pain, we suggest continuing non-opioid therapy rather than a trial of opioids (**Weak recommendation, Low quality evidence**).

Rationale: Low quality evidence suggests a possible appreciable increase in the very serious adverse outcomes of unintentional non-fatal overdose and death in patients with using opioids.

6 & 7. For patients with chronic non-cancer pain beginning long term opioid therapy, we suggest restricting the prescribed dose to under 50mg morphine equivalents daily (**Weak recommendation, Moderate quality evidence**). We recommend restricting the prescribed dose to under 90mg morphine equivalents daily rather than no upper, or a higher limit on dosing (**Strong recommendation, Moderate quality evidence**).

> Remark: The weak recommendation to restrict the prescribed dose to under 50mg morphine equivalents daily acknowledges that there are likely to be some patients who would be ready to accept the increased risks associated with a dose over 50mg to potentially achieve improved pain control. Further, some patients may gain important benefit over 90mg morphine equivalents, but not on lower doses. Referral to a colleague for a second opinion regarding the possibility of increasing above 90mg morphine equivalents daily may therefore be warranted in some individuals.

Rationale: Observational study results provide moderate quality evidence of a progressive increase in the likelihood of unintentional non-fatal overdose or death as the prescribed dose of opioids increases. These serious outcomes are very rare in those prescribed less than 50 morphine equivalents daily, but increase in those prescribed doses of 50 to 90, and though still rare, are very concerning in those prescribed doses of over 90.

8. For patients with chronic non-cancer pain currently using 90mg morphine equivalents of opioids per day or more, with persistent problematic pain and/or problematic side-effects, we suggest rotation to other opioids rather than keeping the opioid the same (**Weak recommendation, Low quality evidence**).

> Remark: Rotation in such patients may be done in parallel with, and as a way of facilitating, dose reduction.

Rationale: Low quality evidence suggests that substitution of an alternative opioid can reduce pain and adverse effects in patients with chronic non-cancer pain using opioids.

9. For patients with chronic non-cancer pain currently using 90mg morphine equivalents of opioids per day or more, we suggest tapering opioids to the lowest

possible dose, including discontinuation, rather than no change in opioid therapy (**Weak recommendation, Low quality evidence**).

> Remark: Some patients are likely to experience significant increase in pain or decrease in function that persist more than one month after a small dose reduction; tapering may be paused and potentially abandoned in such patients.

Rationale: Reduction in opioid dose may reduce adverse effects including cognitive impairment and the likelihood of non-fatal or fatal unintentional overdose. Reduction, particularly if not done very slowly, may cause increased pain, decreased function, or highly aversive symptoms of opioid withdrawal.

10. For patients with chronic non-cancer pain using opioids and experiencing serious challenges in tapering, we recommend a formal multidisciplinary program (**Strong recommendation, Moderate quality evidence**).

> Remark: Recognizing the cost of formal multidisciplinary opioid reduction programs and their current limited availability/capacity, an alternative is a coordinated multidisciplinary collaboration including several health professionals (possibilities include, but are not limited to, a primary care physician, a pharmacist, a physical therapist, a kinesiologist, a psychiatrist, and a psychologist).

Rationale: Studies provide moderate quality evidence that, in patients desiring a reduction or discontinuation of opioid therapy but experiencing serious challenges in tapering or discontinuing therapy, multi-disciplinary programs can substantially increase the likelihood of successful reduction or discontinuation.

* In general, GRADE discourages strong recommendations when the quality of evidence for critical outcomes is low or very low. There are, however, five paradigmatic situations in which strong recommendations may be warranted despite low or very low quality of evidence. One of these is when low quality evidence suggests equivalence of two alternatives, but high quality evidence suggests greater harm of one. For recommendation 1, low quality evidence, much of it indirect, suggests equivalence of opioid therapy and a number of other interventions, and high quality evidence demonstrates greater harm. Another situation is when when high quality evidence suggests modest benefits and low or very low quality evidence suggests possibility of catastrophic harm. For recommendation 3, high quality evidence suggests modest benefit and low quality evidence suggests an elevated risk of serious harm.