Appendix 1 (as submitted by the authors): Example from the *Canadian Guideline* - Recommendation 9 (Optimal Dose)

R09 Recommendation Statement

R09	When conducting a trial of opioid therapy, start with a low dosage, increase dosage gradually and monitor opioid effectiveness until optimal dose is attained. (Grade C).	***Optimal dose***

R09 Discussion

1. Optimal Dose

1.1 Dose: Initial and Incremental

The object of the trial is to determine the optimal dose, i.e., a dose that will improve function or reduce pain intensity by at least 30% without causing major adverse effects or complications. It is recommended to start the opioid trial with a low dose and increase the dose in small quantities. Opioids produce a graded analgesic response: the patient experiences the greatest benefits at lower doses and a plateauing of analgesic response at higher doses. Therefore, slow titration 1) avoids unnecessarily high doses, and 2) reduces the risk of sedation and overdose as it ensures that a dose increase does not exceed the patient's tolerance. (Consider a three-day "tolerance check" for elderly and other high-risk patients: the nurse, physician, or pharmacist calls the patient/family three days after starting the prescription to check for any signs of sedation.) See Table B-9.1 for opioid suggested initial dose and titration.

1.2 Attaining Optimal Dose

The **optimal dose** is reached with a BALANCE of three factors:
1) **effectiveness**: improved function or at least 30% reduction in pain intensity
2) **plateauing**: effectiveness plateaus—increasing the dose yields negligible benefit, and
3) **adverse effects/complications**: adverse effects or complications are manageable.

1.3 Watchful Dose

Watchful Dose = morphine or equivalent dose exceeding 200 mg/day. See Recommendation 10 for guidance on a watchful dose.

2. Measuring Opioid Effectiveness

Opioid effectiveness = improved function or at least 30% reduction in pain intensity.

During an opioid trial, schedule patient visits frequently (e.g., 2–4 weeks) to assess for changes in pain intensity and function.

2.1 Assessing Function Change

The patient's progress in reaching agreed-on goals is an important indicator of function change. Self-report can be prompted by asking about work, household activity, mood, walking ability, sleep, and social activities. For an example of a structured assessment tool frequently used in trials, see Appendix B-9: Brief Pain Inventory.

2.2 Assessing Pain Change

A 30% or greater reduction in pain intensity is considered clinically significant (Farrar 2001).

Appendix to: Furlan AD, Reardon R, Weppler C. Opioids for chronic noncancer pain: a new Canadian practice guideline. *CMAJ* 2010. DOI:10.1503/cmaj.100187.

Change in pain intensity can be assessed using an 11-point (0–10) numeric rating scale (NRS). With each dose increase, the patient should be asked to estimate the pain intensity: a desirable response is a reduction in pain intensity (e.g., from 9/10 [baseline] to 6/10 [endpoint]) and a longer duration of analgesia per dose.

Example of assessing change in pain intensity:

1. Determine the ***raw change*** in the NRS score:
   baseline – endpoint, e.g., 9 – 6 = 3

2. Determine the ***percent change***:

$$\frac{\text{raw change}}{\text{baseline}} \text{ x 100, e.g., } \frac{3}{9} \text{ x 100} = 33\%$$

3. Monitoring for Adverse Effects, Medical Complications, Compliance, and Risks

3.1 Adverse Effects and Medical Complications

See Recommendation 5 for potential adverse effects, medical complications, and risks.

3.2 Compliance

Compliance is indicated when the patient takes the opioids as prescribed and shows no signs of misuse or aberrant drug-related behaviours.

4. Ending Titration

Titration ends when 1) the optimal dose is attained, or the 2) trial is considered a "failed trial."

The following circumstances could indicate a failed trial:

1) The patient experiences insufficient analgesia after two or three dose increases and/or unacceptable adverse effects and/or medical complications (see Recommendation 13).
2) There are indications of misuse or addiction (see Recommendation 12).

5. Documenting the Trial

It is important to record all aspects of the opioid trial in the patient's chart. Details regarding dose, frequency, opioid effectiveness, adverse effects, medical complications, goal attainment, and compliance are crucial in evaluating the opioid trial outcome.

For documentation templates, see Appendix B-7.

R09 Summary of Peer-Reviewed Evidence

1. Clinically important change for numerical pain scale (NRS)

"On average, a reduction of approximately two points or a reduction of approximately 30% in the PI-NRS represented a clinically important difference. The relationship between percent change and the PGIC was also consistent regardless of baseline pain, while higher baseline scores required larger raw changes to represent a clinically important difference" (Farrar 2001).

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