

Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain

Canadian Pain Society Conference

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Background

- Existing guidelines limited or outdated
- Physicians seeking guidance and support
- Concerns about opioid misuse:
 - Increases in prescribing corresponding with increases in abuse, serious injuries and overdose deaths.
 - Canada is the world's third-largest opioid analgesic consumer

Guideline Development

- National Opioid Use Guideline Group (NOUGG)
 - 18 representatives:
 - Canadian Medical Regulatory Authorities
 - Federal Medical Regulatory Authorities of Canada (FMRAC)
 - Oversee guideline development and implementation

Guideline Development - Goals

Short-term Goals:

Create a quality guideline:

- methodologically rigorous
- clinically relevant
- feasible



Mid-term Goals:

Actively move guideline to practice:

- nationally sharable clinician tools;
- teaching/learning resources
- patient/public education resources



Long-term Goals:

- Find academic 'home for the guideline
- evaluate the impact on practice

Guideline Development

- Two year process
- Collaborative effort involving:
 - National Opioid Use Guideline Group (NOUGG)
 - Research team (academic experts)
 - National Advisory Panel (NAP)
 - National Faculty

Guideline Development

- Research Team
 - Literature review
 - Data extraction
 - Drafted recommendations for review

Guideline Development

- National Advisory Panel
 - Nearly 50 individuals from across Canada
 - Review recommendations, develop consensus
 - Group included:
 - Pain specialists
 - Addiction experts
 - Pharmacists
 - Academics
 - Nurses,
 - Patient group representatives

Guideline Implementation

- National Faculty
 - Eight national organizations
 - Clinicians, educators, researchers
 - Responsible for:
 - Guideline implementation
 - Implementation and evaluation strategy

Measurement of Guideline Impact

- Dr. Michael Allen, Dalhousie University
 - National online survey of family physicians
 - Assess how they manage opioid Rx in CNCP
- Dr. Andrea Furlan, studying physiatrist practice and attitude toward opioid use in CNCP

Chronic Non-Cancer Pain (CNCP)

- 38% of institutionalized seniors in Canada experienced pain on a regular basis, compared with 27% of seniors living in households. (Ramage-Morin 2009)
- Osteoarthritis affects 3 million Canadians (www.arthritis.ca)
- A study suggests that 1 million Canadians live with neuropathic pain. (Moulin 2007)
- A general population telephone interview conducted in Canada showed that 25% of the respondents live with CNCP (Boulanger 2007)

Opioid overdose, misuse, and addiction

Canada is currently the world's third-largest opioid analgesic consumer. In Ontario, oxycodone prescriptions rose by 850% from 1991 to 2007, from 23 prescriptions/1000 individuals per year to 197/1000 per year, and the average amount per prescription of long-acting oxycodone increased from 1830 mg to 2280 mg. (Dhalla 2009)

The increase in opioid prescribing has been accompanied by simultaneous increases in abuse, serious injuries, and overdose deaths among individuals taking these drugs (Kuehn 2007).

From 1991 to 2004 in Ontario, the mortality rate due to unintentional opioid overdose increased from 13.7/million to 27.2/million/year, more than double the mortality rate from HIV (12/million) (Dhalla, 2009).

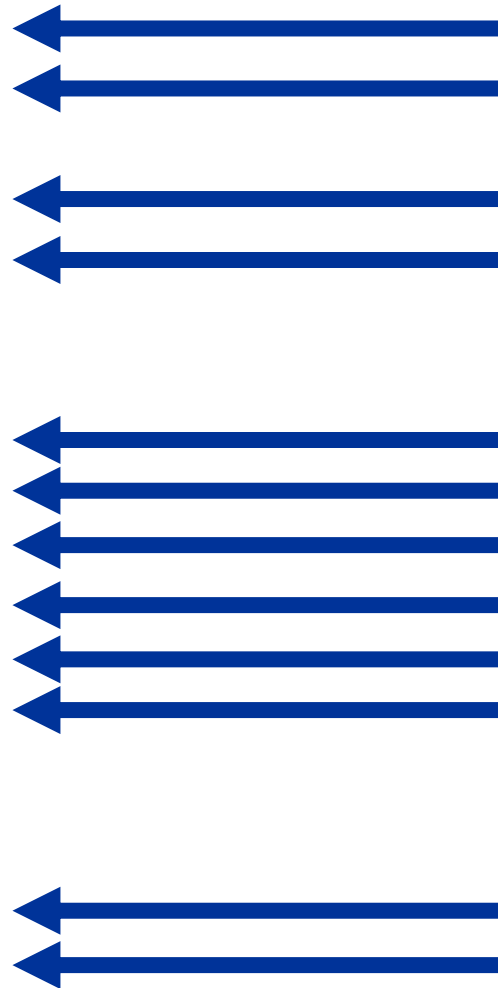
Guideline Development

- **NOUGG** – responsible for overseeing Guideline development
- **Research team** – search literature; extract data; synthesize evidence into proposed recommendations for practice
- **National Advisory Panel** – ~ 50 individuals; review recommendations and develop consensus; provide feedback for Guideline revision
- **National Faculty** – 8 national organizations; clinicians, educators, researchers. Define targeted outcomes for Guideline implementation; Develop implementation & evaluation strategy

Systematic Reviews

Stakeholders

- **Stage 1 – Planning**
 - Identify stakeholders
 - Scope of topics
 - Adequacy of existing reviews
 - Preparing a proposal (resources)
 - Developing a review protocol
- **Stage 2 – Completing**
 - Step 1: Develop question
 - Step 2: Conduct literature search
 - Step 3: Identify relevant studies
 - Step 4: Quality appraisal
 - Step 5: Data extraction
 - Step 6: Evidence synthesis
- **Stage 3 – Reporting & Disseminating**
 - Report and conclusions
 - Dissemination
 - Implementation (if appropriate)



1. Conduct literature search

- ❖ MEDLINE (1960 to July 2009), EMBASE (1988 to July 2009), the Cochrane Database of Systematic Reviews, the Cochrane Controlled Trials Register (CENTRAL), the ACP Journal Club and DARE (May 2005) using the OVID interface
- ❖ Search strategies used for MEDLINE and Embase were the same used in the original meta-analysis. (Furlan 2006)
- ❖ reviewed the reference lists in retrieved articles, reviews and textbooks.

2. Identify relevant publications

Multiple sets of reviewers screened titles and abstracts using the following criteria:

- ❖ Study characteristics: RCTs in humans published in: English, French, Portuguese or Spanish.
- ❖ Population: CNCP defined as pain for more than 6 months. We excluded migraines, dental pain, ischemic pain due to vascular disease and abdominal pains (i.e., chronic pancreatitis, kidney stones, etc.)
- ❖ Interventions: Any opioid given via oral, transdermal, transmucosal or rectal route for at least 7 days. We excluded comparisons of different opioids
- ❖ Outcomes: Only pain (intensity or pain relief), function and side effects were extracted.

Methods (cont'd)

3. Quality appraisal

- ❖ The methodological quality was assessed by two independent reviewers that met to reach consensus.
- ❖ In case of disagreement a third reviewer was consulted.
- ❖ We used the instrument by Jadad et al, which consists of three questions regarding the method of randomization, double-blinding and withdrawals
- ❖ The total score can range from zero to five.
- ❖ Studies scoring three or more were considered “high-quality”, and those having two or less points were considered “low-quality”.

4. Meta-analyses

- ❖ Meta-analyses and meta-regression were conducted using Comprehensive Meta Analysis®
- ❖ All meta-analyses were conducted using a random effects model, and meta-regression was conducted using a fixed effects model.
- ❖ Subgroups were decided a priori to assess the variations in effect sizes.
- ❖ The effect sizes were classified into small (≤ 0.5), medium (0,5 to <0.8) and large (≥ 0.8)

5. Evidence synthesis

- ❖ Stakeholder input recommendations

Methods (cont'd)

6. Recommendations were graded using a system adapted from the “Canadian Task Force on Preventive Health Care Levels of Evidence and Recommendation Grading”

Grade A = Good evidence to include.
Supported by evidence from RCT(s).

Grade B = Fair evidence to include.

- Evidence from controlled trial(s) without randomization, or,
- Evidence from cohort or case-control analytic studies, preferably from more than one centre or research group, or
- Evidence from comparisons between times or places with or without the intervention; dramatic results in uncontrolled experiments could be included here.

Grade C = Consider including.

Supported by opinion of the National Advisory Panel.

Results

- 184 studies
 - 62 Randomized Trials
 - 122 Observational Studies
- 4 modified Delphi rounds

Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain

Part A: Executive Summary and Background
Part B: Recommendations for Practice

PART A

Executive Summary and Background

Published by the
National Opioid Use Guideline Group (NOUGG)
a collaboration of:

- Federation of Medical Regulatory Authorities of Canada
- College of Physicians & Surgeons of British Columbia
- College of Physicians & Surgeons of Alberta
- College of Physicians and Surgeons of Saskatchewan
- College of Physicians and Surgeons of Ontario
- Collège des médecins du Québec
- College of Physicians and Surgeons of New Brunswick
- College of Physicians and Surgeons of Nova Scotia
- College of Physicians and Surgeons of Prince Edward Island
- Government of Nunavut
- Yukon Medical Council

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<http://nationalpaincentre.mcmaster.ca/opioid/>

CMAJ

REVIEW

Opioids for chronic noncancer pain: a new Canadian practice guideline

Andrea D. Furlan MD PhD, Rhoda Reardon Dip(P&OT), Clarence Wepler BSc Pharm, for the
National Opioid Use Guideline Group (NOUGG)

Underestimated chronic noncancer pain and growing misuse of opioids are two challenges presented by opioid therapy. A new Canadian guideline addresses these challenges with recommendations and tools for safe and responsible selection, prescription, initiation and monitoring of opioids.

Chronic noncancer pain is a substantial public health problem in many societies, where it has tremendous negative impact both socially and economically. The most potent analgesics available, opioids have been shown to reduce pain in functional osteoarthritis and neurologic causes.¹ Their efficacy in functional outcomes has been less obvious. Although some physicians are reluctant to prescribe opioids for chronic noncancer pain, Canadian prescribing trends for chronic noncancer pain increased by about 50% between 2000 and 2004,² a rate of increase greater than that of the United States during the same period. Canada is currently the world's sixth-largest supplier of opioid analgesics.³ The increase in opioid prescribing has been accompanied by increases in misuse, abuse, serious injuries and overdoses (related deaths among people taking these drugs).⁴

- Key points**
- In patients with chronic noncancer pain, opioids may be effective and should be considered.
 - Opioid therapy should begin with setting of realistic goals with the patient, a monitored trial of dosage titration, and follow-up to ensure opioid effectiveness.
 - Prescribers and dispensers can minimize potential harms to patients, monitoring use over time, and reducing or stopping opioids when indicated.
 - Good communication and collaboration between health care providers and patients, across clinical disciplines, and between primary care and specialty care is important when treating patients with chronic noncancer pain.

than six months⁵ in male and female adolescents and adults, and is targeted to primary-care physicians, and medical and surgical specialists who manage patients with chronic noncancer pain. Fractures, trauma, and diabetes may also find it useful. The scope of the guideline does not include use of opioids for acute pain or end-of-life pain, or treatment modalities and approaches for chronic noncancer pain other than opioids.

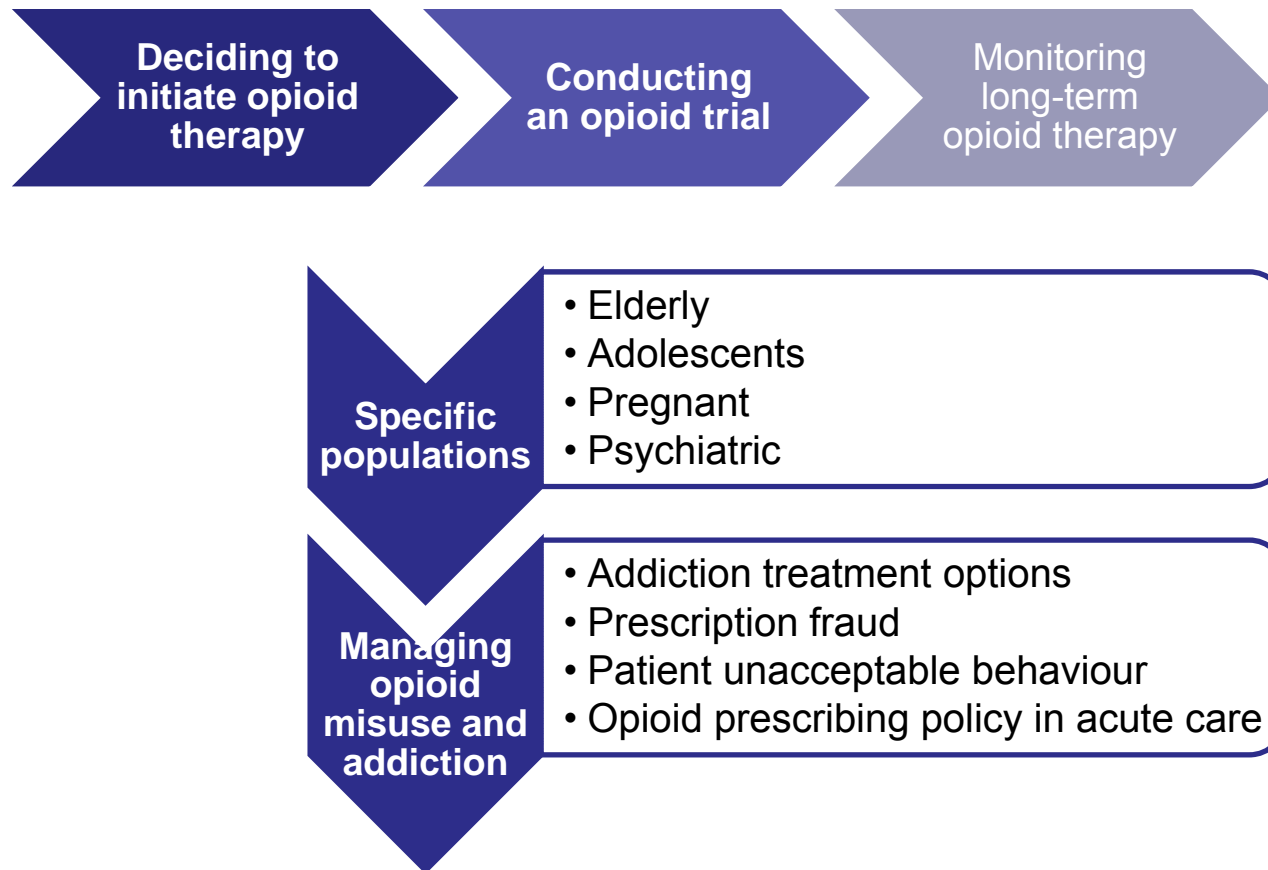
Development

Leadership
Three groups were instrumental in developing the Canadian guideline for safe and effective use of opioids for chronic noncancer pain. These groups were the National Opioid Use Guideline Group, a research group, and a national advisory panel. The role of the National Opioid Use Guideline Group was to oversee the development and implementation of the guideline; the group's members were representatives of regulatory bodies. The research group conducted a research literature review, a physician-epidemiologist and four physician-researchers. This group was responsible for literature reviews.

from the Institute for Work and Health, Toronto Rehabilitation Institute and the Department of Health, University of Toronto; Jennifer Dowling, Management Division, College of Pharmacy and Behavioural Science, University of Toronto; and the physician-researchers, Practices for Health, College of Physicians & Surgeons of Ontario, Hamilton, Ontario, Canada.

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An overview of the Guideline's recommendations



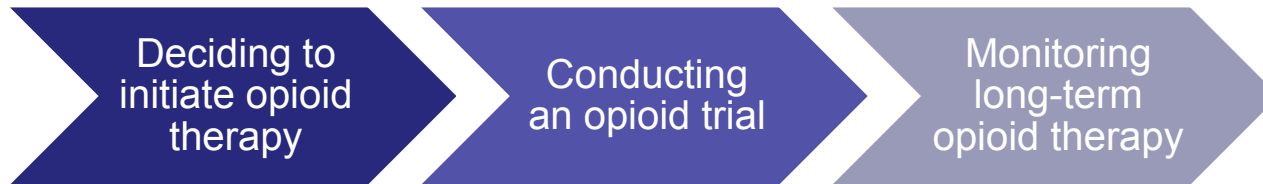
An overview of the Guideline's recommendations



Cluster 1

“Comprehensive assessment”, “Addiction-risk screening”, “Urine drug screening”, “Opioid efficacy”, “Risks, adverse effects, complications”, “Benzodiazepine tapering”

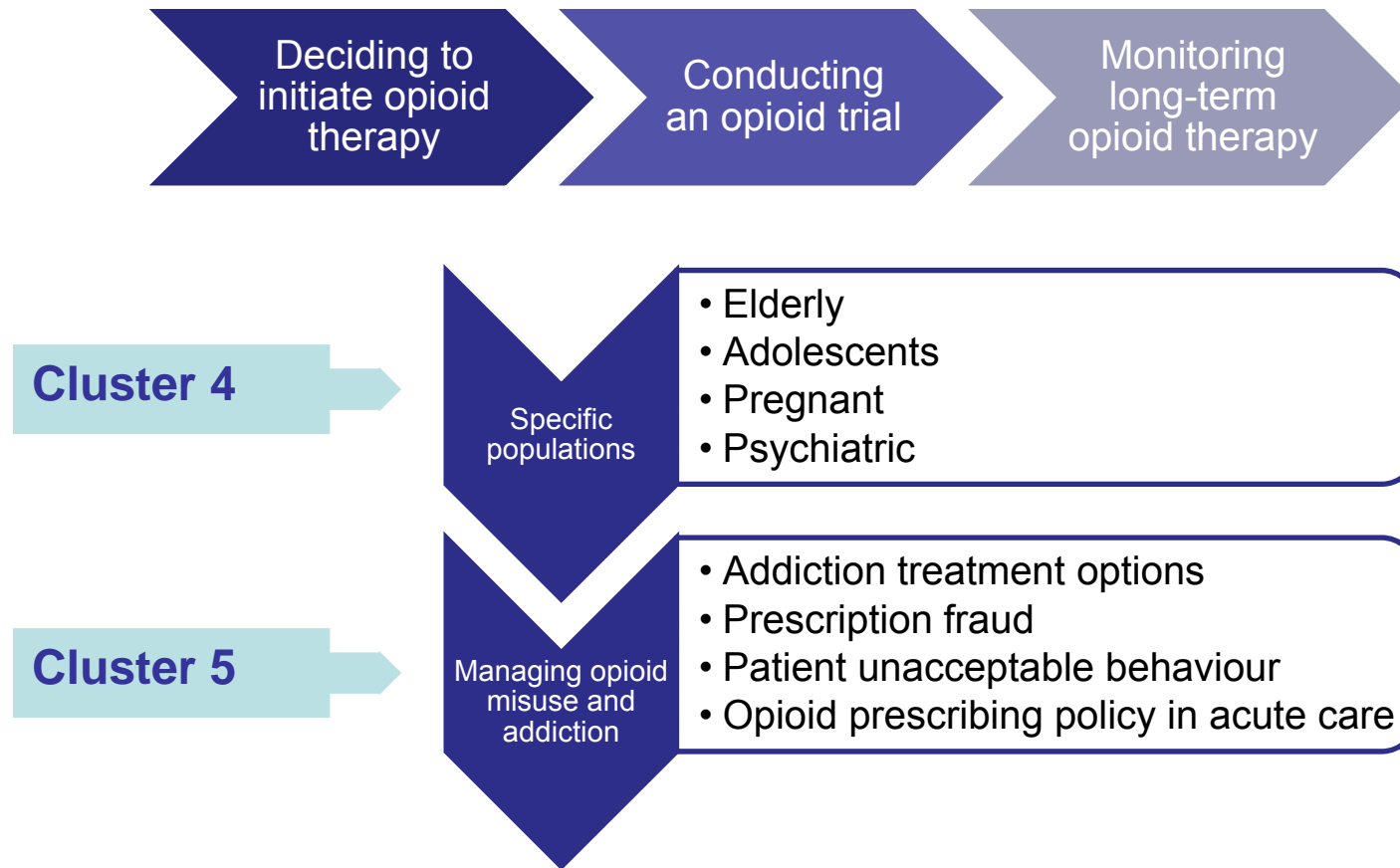
An overview of the Guideline's recommendations



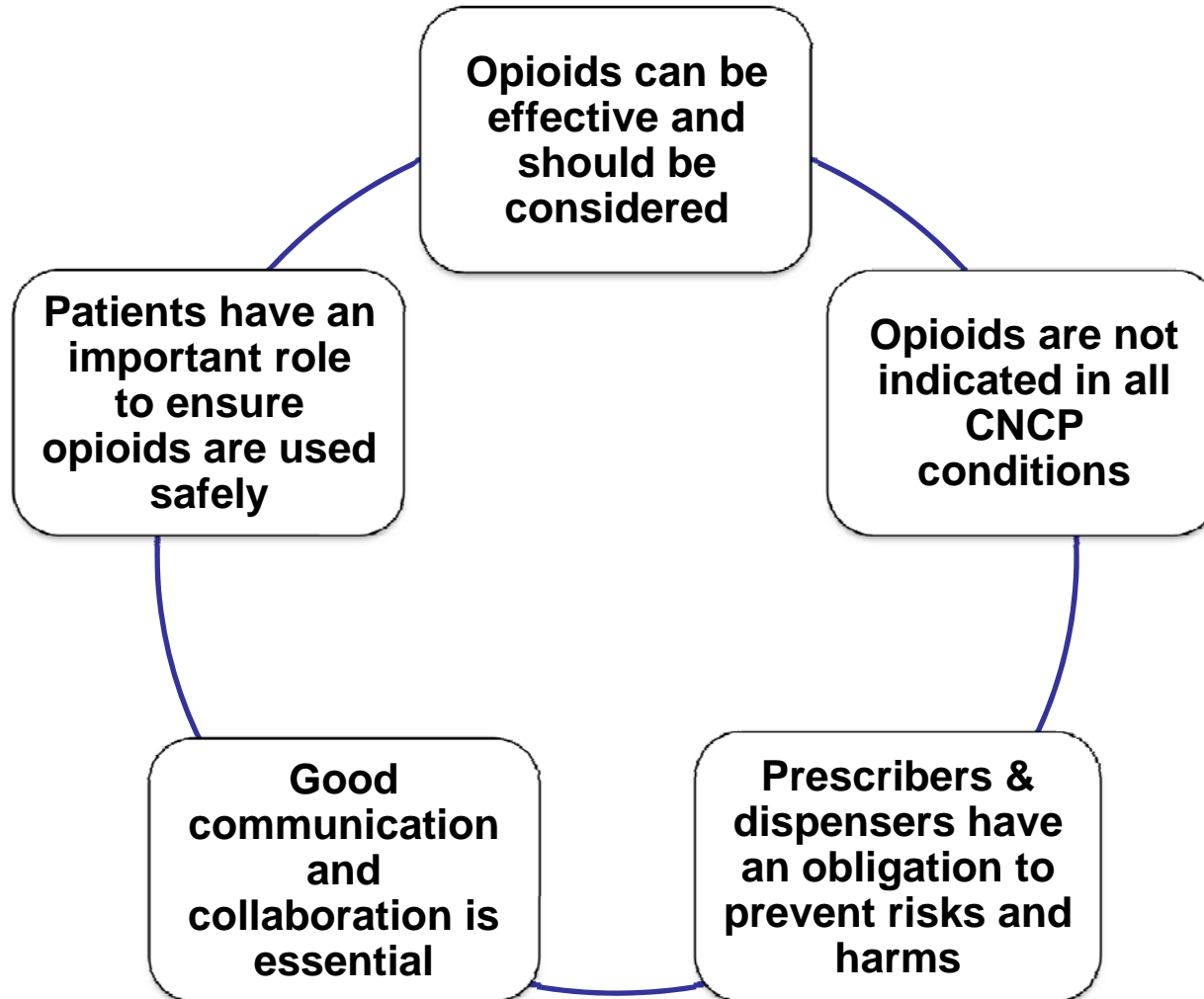
Cluster 2

“Titration and driving”, “Stepped opioid selection”, “Optimal dose”, “Watchful dose”, “Risk: opioid misuse”

An overview of the Guideline's recommendations



An overview of the Guideline's recommendations



Recommendations Address Key Clinical Questions

- 1. What should I consider before writing an opioid prescription?*
- 2. How do I titrate the opioid dose?*
- 3. What should I do to ensure patient safety?*
- 4. When do I stop the patient's opioids?*

1. What should I consider before writing an opioid prescription?

- Complete a thorough assessment to:
 - understand the pain problem
 - make an informed decision about opioids as a reasonable treatment choice.
- Consider if screening tools are needed to help identify patients at risk of opioid misuse or addiction.

... cont'd

1. What should I consider before writing an opioid prescription?

- Manage patient expectations by setting functional improvement and pain-reduction goals with the patient - these become the outcomes to measure effectiveness of opioid therapy.
- Ensure informed consent by reviewing with the patient potential benefits, risks, side effects, and complications of opioid therapy.

2. *How do I titrate the opioid dose?*

- Start with a low dose, increase gradually and monitor “**analgesic effectiveness**”
 - e.g. an improvement in function, or a reduction in pain intensity of at least 30%

... cont'd

2. How do I titrate the opioid dose?

- Track the daily dose in morphine equivalents and flag the “**watchful dose.**”
 - e.g. 200 mg morphine or equivalent per day
Note: most patients can be effectively managed below this.
- If you determine the dose required is beyond the watchful dose:
 - reassess the pain problem to ensure opioids are the right therapy
 - reassess risk of misuse
 - increase monitoring vigilance

... cont'd

2. How do I titrate the opioid dose?

- Recognize the “**optimal dose**” is reached when there is a balance of three factors:
 1. the opioid is effective
e.g. improved function or at least 30% reduction in pain intensity,
 2. effectiveness plateaus
e.g. increasing the dose yields little increased analgesic benefit, and
 3. there are no major side effects or complications.

3. What should I do to ensure patient safety?

- Use the functional and pain reduction goals set with the patient to monitor if opioids are effective - structured assessment tools might also help.
- Watch for aberrant drug-related behaviours that could signal opioid misuse — tools can help.

... cont'd

3. What should I do to ensure patient safety?

- Assess factors that could impair cognition and psychomotor ability, possibly making driving unsafe.
- Use available consultation as needed:
 - pain condition unresponsive
 - opioid misuse or addiction suspected
 - special populations:
 - pregnant, psychiatric co-morbid conditions, elderly, or adolescent.
- Collaborate with pharmacists to improve patient education and safety.

4. When do I stop the patient's opioids?

- Stop or switch opioids when side effects or risks are unacceptable, or analgesic effectiveness is insufficient.
- Discontinue opioids with a tapering protocol
 - Avoid sedative-hypnotic drugs, especially benzodiazepines, during the taper.

Guideline Implementation – National Strategies

- Journal publication
- Conferences
- Academic detailing
- Workshops
- Website Resources
 - Michael G. DeGroote Pain Centre
(McMaster University)
<http://nationalpaincentre.mcmaster.ca/opioid/>
- Public Education

OPIOID MANAGER

The Opioid Manager is designed to be used as a point of care tool for providers prescribing opioids for chronic non-cancer pain. It condenses key elements from the Canadian Opioid Guideline and can be used as a chart insert.

A Before You Write the First Script

Patient Name: _____

Pain Diagnosis: _____

Date of Onset: _____

Goals decided with patient:

Initiation Checklist

	Y	N	Date
Are opioids indicated for this pain condition			
Explained potential benefits			
Explained adverse effects			
Explained risks			
Patient given information sheet			
Signed treatment agreement (as needed)			
Urine drug screening (as needed)			

Opioid Risk Tool

By Lynn R. Webster MD

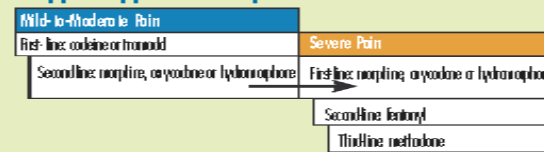
Item (circle all that apply)	Item score if female	Item score if male
1. Family History of Substance Abuse:		
Alcohol	1	3
Illegal Drugs	2	3
Prescription Drugs	4	4
2. Personal History of Substance Abuse:		
Alcohol	3	3
Illegal Drugs	4	4
Prescription Drugs	5	5
3. Age (mark box if 16-45)	1	1
4. History of Preadolescent Sexual Abuse	3	0
5. Psychological Disease (Attention Deficit Disorder, Obsessive-Compulsive Disorder, or Bipolar), Schizophrenia, Depression	2	2
Depression	1	1
Total		

Total Score Risk Category:
Low Risk: 0 to 3, Moderate Risk: 4 to 7, High Risk: 8 and above

Overdose Risk

Patient factors	Provider factors	Opioid factors	Other factors
<ul style="list-style-type: none"> Elderly On benzodiazepines Renal impairment Hepatic impairment COPD Sleep apnea Sleep disorders Cognitive impairment 	<ul style="list-style-type: none"> Incomplete assessments Rapid titration Combining opioids and sedating drugs Failure to monitor dosing Inefficient information given to patient and/or relatives 	<ul style="list-style-type: none"> Codine & Tramadol - lower risk CR Formulations - higher doses than IR Prevention Assess for Risk Factors Educate patients/families about risks & prevention 	<ul style="list-style-type: none"> Start low, titrate gradually, monitor frequently Careful with long-acting opioids Higher risk of overdose - reduce initial dose by 50%, titrate gradually Avoid potentiated routes Adolescents, elderly - may need consultation Watch for misuse

Stepped Approach to Opioid Selection



B Initiation Trial

A closely monitored trial of opioid therapy is recommended before deciding whether a patient is prescribed opioids for long-term use.

Suggested Initial Dose and Titration (Modified from Weaver M, 2007 and the eCPS, 2008) Notes: The table is based on dosing for OMP. Brand names are shown if there are some distinct features about specific formulations. Reference to brand names as examples does not imply endorsement of any of these products. CR = controlled release, IR = immediate release, NA = not applicable, ASA = Acetylsalicylic Acid

Opioid	Initial dose	Minimum time interval for increase	Suggested dose increase	Minimum daily dose before converting IR to CR
Codine (alone or in combination with acetaminophen or ASA)	15-30 mg q 4 h as needed	7 days	15-30 mg/day up to maximum of 600 mg/day (acetaminophen dose should not exceed 3.2 grams/day)	100 mg
CR Codine	90 mg q 12 h	2 days	90 mg/day up to maximum of 300 mg q 12 h	NA
Tramadol (37.5 mg) + acetaminophen (325 mg)	1 tablet q 4-6 h as needed up to 4/day	7 days	12 tabs q 4-6 h as needed up to maximum 8 tablets/day	3 tablets
CR Tramadol	a) Zydol [®] : 150 mg q 24 h b) Indol [®] : 100 mg q 24 h c) Rolin [®] : 100 mg q 24 h	a) 7 days b) 2 days c) 5 days	Maximum doses of 400 mg/day (b) 300 mg/day (c) 300 mg/day	NA
IR Morphine	5-10 mg q 4 h as needed maximum 40 mg/day	7 days	5-10 mg/day	20-30 mg
CR Morphine	10-30 mg q 12 h Kadian [®] : q 24 h Kadian [®] should not be started in opioid-naïve patients	Minimum 2 days, recommended 1-3 days	5-10 mg/day	NA
IR Oxycodone	5-10 mg q 6 h as needed maximum 30 mg/day	7 days	5 mg/day	20 mg
CR Oxycodone	10-20 mg q 12 h maximum 30 mg/day	Minimum 2 days, recommended 1-3 days	10 mg/day	NA
IR Hydrocodone	1-2 mg q 4-6 h as needed maximum 8 mg/day	7 days	1-2 mg/day	6 mg
CR Hydrocodone	3 mg q 12 h maximum 9 mg/day	Minimum 2 days, recommended 1-3 days	2-4 mg/day	NA

Initiation Trial Chart

Date	D/M/Y	D/M/Y	D/M/Y	D/M/Y
Opioid prescribed				
Daily dose				
Daily morphine equivalent				
400				
300				
200				
100				
Goals achieved → Yes, No, Partially				
Pain intensity				
Functional status → Improved, No Change, Worsened				
Adverse effects				
Nausea				
Constipation				
Drowsiness				
Dizziness/Vertigo				
Dry skin/Pruritis				
Vomiting				
Other?				
Complications?				
(Reviewed: Y/N)				
Other Monitoring				

To access the Canadian Guideline for Safe and Effective Use for Non-Chronic Cancer Pain, to download the Opioid Manager and to provide feedback visit <http://nationalpaincentre.mcmaster.ca/opioid/>

Maintenance & Monitoring

Morphine Equivalence Table

Opioid	Equivalent Doses (mg)	Conversion to MEQ
Morphine	30	1
Codeine	200	0.15
Oxycodone	20	1.5
Hydromorphone	6	5
Meperidine	300	0.1
Methadone & Tramadol	Dose Equivalents unreliable	
Transdermal fentanyl	60 – 134 mg morphine = 25 mcg/h	
	135 – 179 mg = 37 mcg/h	
	180 – 224 mg = 50 mcg/h	
	225 – 269 mg = 62 mcg/h	
	270 – 314 mg = 75 mcg/h	
	315 – 359 mg = 87 mcg/h	
360 – 404 mg = 100 mcg/h		

Switching Opioids:	
If previous opioid dose was:	Then, SUGGESTED new opioid dose is:
High	50% or less of previous opioid (converted to morphine equivalent)
Moderate or low	60-75% of the previous opioid (converted to morphine equivalent)

Maintenance & Monitoring Chart

Date	D/M/Y	D/M/Y	D/M/Y	D/M/Y	D/M/Y	D/M/Y
Opioid prescribed						
Daily dose						
Daily morphine equivalent						
400						
300						
200						
100						
Goals achieved → Yes, No, Partially						
Pain intensity						
Functional status → Improved, No Change, Worsened						
Adverse effects						
Nausea						
Constipation						
Drowsiness						
Dizziness/Vertigo						
Dry skin/Pruritis						
Vomiting						
Other?						
Complications? (Reviewed:Y/N)						
Other Monitoring						

0 = None
1 = Limits ADLs
2 = Prevents ADLs

When is it time to Decrease the dose or Stop the Opioid completely?

When to stop opioids	Examples and Considerations
Pain Condition Resolved	Patient receives definitive treatment for condition. A trial of tapering is warranted to determine if the original pain condition has resolved.
Risks Outweighs Benefits	Overdose risk has increased. Clear evidence of diversion. Aberrant drug related behaviours have become apparent.
Adverse Effects Outweighs Benefits	Adverse effects impairs functioning below baseline level. Patient does not tolerate adverse effects.
Medical Complications	Medical complications have arisen (e.g. hypogonadism, sleep apnea, opioid induced hyperalgesia)
Opioid Not Effective	Opioid effectiveness = improved function or at least 30% reduction in pain intensity Pain and function remains unresponsive. Opioid being used to regulate mood rather than pain control. Periodic dose tapering or cessation of therapy should be considered to confirm opioid therapy effectiveness.

How to Stop – the essentials

How do I stop? The opioid should be tapered rather than abruptly discontinued.

How long will it take to stop the opioid? Tapers can usually be completed between 2 weeks to 4 months.

When do I need to be more cautious when tapering? Pregnancy: Severe, acute opioid withdrawal has been associated with premature labour and spontaneous abortion.

How do I decrease the dose? Decrease the dose by no more than 10% of the total daily dose every 1-2 weeks. Once one-third of the original dose is reached, decrease by 5% every 2-4 weeks. Avoid sedative-hypnotic drugs, especially benzodiazepines, during the taper.

Aberrant Drug Related Behaviour* (Modified by Passik, Kirsh et al 2002).

Indicator	Examples
*Altering the route of delivery	• Injecting, biting or crushing oral formulations
*Accessing opioids from other sources	• Taking the drug from friends or relatives • Purchasing the drug from the "street" • Double-doctoring
Unsanctioned use	• Multiple unauthorized dose escalations • Binge rather than scheduled use
Drug seeking	• Recurrent prescription losses • Aggressive complaining about the need for higher doses • Harassing staff for faxed scripts or fit-in appointments • Nothing else "works"
Repeated withdrawal symptoms	• Marked dysphoria, myalgias, GI symptoms, craving
Accompanying conditions	• Currently addicted to alcohol, cocaine, cannabis or other drugs • Underlying mood or anxiety disorders not responsive to treatment
Social features	• Deteriorating or poor social function • Concern expressed by family members
Views on the opioid medication	• Sometimes acknowledges being addicted • Strong resistance to tapering or switching opioids • May admit to mood-leveling effect • May acknowledge distressing withdrawal symptoms

* = behaviours more indicative of addiction than the others.

Recommendations Address Key Clinical Questions

- 1. What should I consider before writing an opioid prescription?*
- 2. How do I titrate the opioid dose?*
- 3. What should I do to ensure patient safety?*
- 4. When do I stop the patient's opioids?*