Canadian guideline for safe and effective use of opioids for chronic noncancer pain

Clinical summary for family physicians. Part 2: special populations

Meldon Kahan MD MHSc CCFP FRCPC **Lynn Wilson** MD CCFP FCFP **Angela Mailis-Gagnon** MD MSc FRCPC **Anita Srivastava** MD MSc CCFP

Abstract

Objective To provide family physicians with a practical clinical summary of opioid prescribing for specific populations based on recommendations from the Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain.

Quality of evidence Researchers for the guideline conducted a systematic review of the literature, focusing on reviews of the effectiveness and safety of opioids in specific populations.

Main message Family physicians can minimize the risks of overdose, sedation, misuse, and addiction through the use of strategies tailored to the age and health status of patients. For patients at high risk of addiction, opioids should be reserved for well-defined nociceptive or neuropathic pain conditions that have not responded to first-line treatments. Opioids should be titrated slowly, with frequent dispensing and close monitoring for signs of misuse. Suspected opioid addiction is managed with structured opioid therapy, methadone or buprenorphine treatment, or abstinence-based treatment. Patients with mood and anxiety disorders tend to have a blunted analgesic response to opioids, are at higher risk of misuse, and are often taking sedating drugs that interact adversely with opioids. Precautions similar to those for other high-risk patients should be employed. The opioid should be tapered if the patient's pain remains severe despite an adequate trial of opioid therapy. In the elderly, sedation, falls, and overdose can be minimized through lower initial doses, slower titration, benzodiazepine tapering, and careful patient education. For pregnant women taking daily opioid therapy, the opioids should be slowly tapered and discontinued. If this is not possible, they should be tapered to the lowest effective dose. Opioid-dependent pregnant women should receive methadone treatment. Adolescents are at high risk of opioid overdose, misuse, and addiction. Patients with adolescents living at home should store their opioid medication safely. Adolescents rarely require long-term opioid therapy.

Conclusion Family physicians must take into consideration the patient's age, psychiatric status, level of risk of addiction, and other factors when prescribing opioids for chronic pain.

KEY POINTS Patients with chronic noncancer pain vary widely in their response to opioid therapy and their vulnerability to sedation, overdose, and addiction. This review provides a brief clinical summary of the recommendations for specific populations in the recently released Canadian guidelines, including patients at high risk of addiction, those with concurrent mental disorders, elderly patients, adolescents, and pregnant patients. The risks of overdose, sedation, misuse, and addiction can be minimized through strategies such as careful patient selection, slow titration, patient education, frequent dispensing, and urine drug screening.

Prescription opioid addiction and overdose deaths have increased dramatically in North America in the past 10 years, and physicians' prescriptions are an important source of opioids for patients suffering these harms. Of 1095 people who died of opioid-related overdose in Ontario, 56% had been given opioid prescriptions in the 4 weeks before death.[1] In a study of opioid-dependent patients admitted to a medical detoxification facility in Toronto, Ont, 37% received their opioids from doctors' prescriptions, 26% from both a prescription and the street, and only 21% entirely from the street (the remaining 16% took over-the-counter codeine or were given opioids by friends or family).[2]

These and other opioid-related harms can be minimized with an individualized approach to opioid prescribing, tailored to patients' health status and risk factors. Patients with chronic noncancer pain (CNCP) vary greatly in their response to opioids and their risk of complications, influenced by factors such as age, concurrent medication use, psychiatric status, and family history.

This article has been peer reviewed.
Can Fam Physician 2011;57:1269-76

This article is eligible for Mainpro-M1 credits.
To earn credits, go to www.cfp.ca and click on the Mainpro link.

La traduction en français de cet article se trouve à www.cfp.ca dans la table des matières du numéro du novembre 2011 à la page e419.

Purpose

This paper summarizes recommendations made in the Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain for specific population groups: the elderly, adolescents, pregnant patients, patients with comorbid mental illness, and opioid-addicted patients.[3] The complete guideline is available from **nationalpaincentre.mcmaster.ca.** A companion article (**page 1257**) discusses guideline development and opioid prescribing for the general adult population.[4]

Addiction

Prevalence. A recent meta-analysis estimated that 3.3% of CNCP patients taking prescribed opioids were addicted to them, with wide variation among clinics and regions. Aberrant drug-related behaviour, which sometimes indicates addiction, had an estimated prevalence of 11.5%.[5] The prevalence of opioid misuse and addiction is increasing throughout North America,[1,6,7] in parallel with the increase in prescribing of controlled-release opioids.[8] Physician groups, medical regulators, and public health officials are considering various policy options to address the crisis, including physician education, a prescription monitoring system, and expansion of addiction treatment.[9]

Clinical features and diagnosis. Some patients experience a euphoric effect from opioids, described as a feeling of peace or freedom from worry. This effect is independent of the opioid's analgesic effect and only occurs in a small proportion of patients. A patient is said to be "addicted" if he or she repeatedly seeks this euphoric effect despite the difficulties this behaviour creates. Tolerance develops rapidly to the euphoric effects, compelling the addicted patient to seek higher doses of the drug. Eventually the patient experiences frightening withdrawal symptoms at the end of a dosing interval, characterized by insomnia, anxiety, drug craving, and flulike symptoms such as myalgia and nausea. Tolerance and withdrawal might drive the patient to seek higher opioid doses through unsanctioned dose escalation, accessing opioids from other sources, or altering the route of delivery (crushing, snorting, or injecting oral tablets).

The addicted patient is typically depressed and anxious, and might be addicted to other drugs such as alcohol or cocaine. Paradoxically, the patient often reports severe pain despite the high opioid dose, perhaps owing to withdrawal-mediated pain, hyperalgesia, or opioid-induced dysphoria.

Screening. At baseline, all patients should be asked about their current use of alcohol, cannabis, opioids, benzodiazepines, sedating over-the-counter preparations, and street drugs. Their weekly consumption of these substances should be quantified (**Boxes 1** and **2**).[3,10] They should also be asked about past and family histories of problematic substance use. A comprehensive inquiry about substance use is recommended because a history of addiction to any substance (whether opioid or nonopioid) is a risk factor for prescription opioid misuse and addiction. Also, alcohol and other sedating drugs can have dangerous interactions with opioids.

Screening questionnaires can be helpful in determining a patient's risk of opioid misuse and addiction. The Opioid Risk Tool (**Table 1**)[11] is the simplest and most widely used of the screening tools. However, a systematic review concluded that none of the opioid addiction screening tools can be recommended with confidence, because when the tools were tested the samples were small and not representative.[12] Urine drug screening (UDS) can also be considered if it is available (**Tables 2** and **3**),[3,13] particularly if the patient is not well known to the physician or is at higher risk of addiction. Urine drug screening can be of value in both detecting and reducing substance use.[14,15] However, UDS has a high rate of false-negative and false-positive results, and some provinces do not reimburse laboratories for UDS.

An unexpected result on UDS must be accompanied by a careful patient assessment (**Table 4**).[3] For example, the presence of cocaine on UDS could indicate

Box 1. Interview guide for alcohol consumption: *A) Interview questions; B) Low-risk drinking guidelines.*

A)

Use the following screening questions to screen for high-risk alcohol consumption:

1. Men: How many times* in the past year have you had 5 or more drinks at one time?
   Women: How many times* in the past year have you had 4 or more drinks at one time?
2. How many drinks do you consume per week?
3. Have you attended a treatment program for alcohol?
4. Do you have a family history of alcohol or drug problems?

B)

Low-risk drinking guidelines[10]

No more than 2 standard drinks on any 1 day

- Women: up to 9 standard drinks a week
- Men: up to 14 standard drinks a week

Patients who exceed the low-risk drinking guidelines are considered to be at risk of acute problems, such as trauma, or chronic problems, such as depression and hypertension

*Two or more times is considered a positive screen, requiring further assessment. A standard drink is equal to 1 bottle of beer (12 oz of 5% alcohol), a 5-oz glass wine (5 standard drinks in 750-mL wine bottle), 1.5 oz of liquor, such as vodka or scotch (18 standard drinks in 26-oz bottle of 40% alcohol).

Adapted from the National Opioid Use Guideline Group.[3]

Box 2. Interview guide for substance use

1. Cannabis: How many joints do you smoke per day or week?
2. Cocaine: Have you used any cocaine in the past year?
3. Over-the-counter drugs: Do you regularly use over-the-counter medications for sleep or nausea?
4. Opioids:
- In the past year, have you used opioids from any source (eg, over the counter [Tylenol No. 1], prescriptions from other physicians, borrowed from friends or family, or buying from the street)?
- How much did you take and how often?
- Do you crush or inject oral tablets?
- Have you experienced opioid withdrawal symptoms (eg, myalgia, gastrointestinal symptoms, insomnia, or dysphoria)?
- Have you had a previous opioid problem?
- Have you ever attended a treatment program for opioid addiction (eg, methadone clinic)?

5. Benzodiazepines: How much and how often do you take benzodiazepines and where do you get them from?

Reprinted from the National Opioid Use Guideline Group.[3]

Table 1. Opioid Risk Tool: *Check the box if the item applies; a score of 0-3 indicates low risk, a score of 4-7 indicates moderate risk, and a score of 8 or higher indicates high risk.*

ITEM	WOMEN	MEN
1. Family history of substance abuse:		
• alcohol	[ ] 1 point	[ ] 3 points
• illegal drugs	[ ] 2 points	[ ] 3 points
• prescription drugs	[ ] 4 points	[ ] 4 points
2. Personal history of substance abuse:		
• alcohol	[ ] 3 points	[ ] 3 points
• illegal drugs	[ ] 4 points	[ ] 4 points
• prescription drugs	[ ] 5 points	[ ] 5 points
3. Age between 16 and 45 y	[ ] 1 point	[ ] 1 point
4. History of preadolescent sexual abuse	[ ] 3 points	[ ] 0 points
5. Psychological disease		
• attention deficit disorder, obsessive-compulsive disorder, bipolar disorder, or schizophrenia	[ ] 2 points	[ ] 2 points
• depression	[ ] 1 point	[ ] 1 point
Total		

Adapted from Webster and Webster.[11]

Table 2. Immunoassay versus chromatography for detection of opioid use

IMMUNOASSAY	CHROMATOGRAPHY
General immunoassay does not differentiate among various opioids, although immunoassays for specific opioids are now available	Differentiates among codeine, morphine, oxycodone, hydrocodone, hydromorphone, and heroin (monoacetylmorphine)
Will show false-positive results (eg, poppy seeds)	Does not react to poppy seeds
General immunoassay often misses semisynthetic and synthetic opioids (eg, oxycodone, methadone, fentanyl)	More accurate for semisynthetic and synthetic opioids

Reprinted from the National Opioid Use Guideline Group.[3]

Table 3. Detection times for immunoassay and chromatography

	NUMBER OF DAYS DRUG IS DETECTABLE	
DRUG	IMMUNOASSAY	CHROMATOGRAPHY
Benzodiazepines (regular use)	• 20 d or more for regular diazepam use • Immunoassay does not distinguish among benzodiazepines • Intermediate-acting benzodiazepines, such as clonazepam, are often undetected	Not usually used for benzodiazepines
Cannabis	20 d or more	Not used for cannabis
Cocaine and metabolites	3-7 d	1-2 d
Codeine	2-5 d	1-2 d (codeine metabolized to morphine)
Hydrocodone	2-5 d	1-2 d
Hydromorphone	2-5 d	1-2 d
Meperidine	1 d (often missed)	1 d
Morphine	2-5 d	1-2 d; morphine can be metabolized to hydromorphone
Oxycodone	Often missed	1-2 d

Adapted from Brands and Brands.[13]

occasional nonproblematic use or serious addiction. The presence of a nonprescribed opioid could indicate double-doctoring, street use, or "innocent" sharing of medications among family members. The absence of a prescribed opioid could indicate diversion or binge use (causing the patient to run out early).

Depending on the outcome of the assessment, the physician could refer the patient for addiction treatment, increase frequency of UDS, initiate an opioid

Table 4. Interpreting unexpected results of urine drug screening

UNEXPECTED RESULT	POSSIBLE EXPLANATIONS	ACTIONS FOR THE PHYSICIAN
UDS negative for prescribed opioid	• False negative • Noncompliance • Diversion	• Repeat test using chromatography; specify the drug of interest • Before repeating the test take a detailed history of the patient's medication use for the preceding 7 d • Ask patient if they've given the drug to others • If diversion is strongly suspected, assess for addiction to opioids, cocaine, etc; switch, taper, and discontinue the opioid, and refer for addiction treatment
UDS positive for nonprescription opioids or benzodiazepines	• False positive • Patient acquired drugs from other sources	• Ask patient if they accessed opioids from other doctors or acquaintances • Assess for opioid misuse or addiction, and treat accordingly
UDS positive for illicit drugs (eg, cocaine, cannabis)	• False positive • Patient is an occasional user • Patient is addicted to the illicit drug	• Assess for abuse or addiction • Refer for addiction treatment as appropriate • Consider tapering and discontinuing opioids if patient is currently addicted to other drugs (eg, cocaine); consider transferring to methadone or buprenorphine treatment
UDS positive for cannabis	• Patient is a social user • Patient uses it for pain • Patient is addicted to cannabis • Patient has concurrent psychiatric condition	• Ask about cannabis use • If patient is a regular user (4 or more joints a week), advise abstinence or treatment if there is concurrent clinical depression, psychosis, or impairment in functioning, or if the patient is an adolescent
Urine creatinine is lower than 2-3 mmol/L	• Patient added water to sample	• Repeat UDS • Consider supervised collection or temperature testing • Take a detailed history of the patient's medication use for the preceding 7 d • Review and revise the treatment agreement
Urine sample is cold	• Delay in handling sample (urine cools within minutes) • Patient added water to sample	• Repeat UDS • Consider supervised collection or temperature testing • Take a detailed history of the patient's medication use for the preceding 7 d • Review and revise the treatment agreement

UDS—urine drug screening.
Reprinted from the National Opioid Use Guideline Group.[3]

taper, shorten the dispensing interval, or provide additional patient education. In any event, physicians should avoid acting in anger or haste. Punitive actions such as "firing" the patient or abruptly stopping the medication are rarely in the patient's best interest, and can generate patient complaints or lawsuits.

Diagnosis. Diagnosis of addiction can be difficult, as patients are often reluctant to disclose symptoms and behaviour that suggest opioid addiction. Consultation with an addiction medicine physician might be helpful. **Table 5**[3,16] outlines useful diagnostic clues. These include baseline risk factors (eg, psychiatric disorders, strong personal or family history of addiction); an opioid dose that is far in excess of what would normally be required for the particular pain condition; presence of illicit drugs or absence of prescribed drugs on UDS; and aberrant drug-related behaviour (eg, frequently running out early, altering the route of delivery, accessing opioids from multiple sources). While aberrant behaviour often indicates addiction, it is sometimes caused by undertreated pain, cognitive impairment, or other conditions.

Management of high-risk patients. Patients are at higher risk of opioid misuse or addiction if they currently drink more than recommended by the low-risk drinking guidelines, smoke more than 4 cannabis joints per week, use street drugs, or acquire psychoactive prescription drugs from sources other than their physicians. A past history of addiction to any substance is also a serious risk factor, especially if the addiction was recent, prolonged, or severe. Other risk factors include strong family history of addiction, age younger than 40 years, and active mental disorders.

For high-risk patients who are currently misusing or addicted to alcohol, cocaine, or other drugs, opioid therapy should usually be withheld until the addiction is treated and is in remission. Prescribing opioids to patients who are currently addicted to nonopioid drugs increases the risk of drug diversion and of adverse opioid-sedative drug interactions. Furthermore, addiction treatment might render opioid therapy unnecessary, as abstinence or methadone and buprenorphine treatment often improve pain perception, functioning, and mood.

Table 5. Clinical features of opioid misuse and addiction

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 prescriptions or fit-in appointments • Nothing else "works"
Repeated withdrawal symptoms	• Marked dysphoria, myalgias, gastrointestinal symptoms, cravings
Accompanying conditions	• Current addiction 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 • Might admit to mood-leveling effect • Might acknowledge distressing withdrawal symptoms

*This behaviour is more indicative of addiction than the others.
Reprinted from the National Opioid Use Guideline Group[3] and Passik and Kirsh.[16]

While not contraindicated, opioids should be used with caution in CNCP patients with past history of addiction or active mental illnesses. In such cases, opioids should usually be reserved for definitively diagnosed nociceptive or neuropathic pain conditions that have not responded to nonopioid treatments. Codeine or tramadol should be used as first-line agents. If potent opioids are required, morphine is recommended over oxycodone or hydromorphone, as the latter drugs might have a higher abuse liability than equianalgesic doses of morphine.[17-20] The dose should be titrated slowly using small increments, and the maintenance dose should be well below a 200-mg morphine equivalent dose daily. The tablets should be dispensed in small quantities, with a treatment agreement prohibiting early refills. Pill counts and UDS might also be considered.

Management of suspected addiction. The 3 treatment options for suspected opioid addiction are structured opioid therapy (SOT), opioid-agonist treatment, and abstinence-based treatment.

Structured opioid therapy: Structured opioid therapy consists of frequent dispensing of small amounts of the drug, close follow-up for mood and analgesic response, monitoring for aberrant drug-related behaviour through history and UDS, and tapering for patients taking high doses (**Table 6**).[21] Structured opioid therapy should be reserved for addicted patients who do not acquire opioids from the street or other sources, do not alter the route of delivery, and are not currently addicted to other drugs. Patients are often able to hide aberrant behaviour; therefore, physicians should attempt SOT only in patients they have known for several years or longer, who they are confident will not access opioids from other sources, and who have pain conditions that would normally require opioid analgesics. In observational studies and one small controlled trial, SOT has been associated with improved mood and pain scores, increased medication compliance, and increased referral rates for addiction treatment.[14,22-25] These studies were conducted in multidisciplinary clinics involving internists, pharmacists, and nurses, so their relevance to primary care is uncertain. Patients who continue to show aberrant behaviour such as running out early should be referred for opioid-agonist treatment or abstinence-based treatment.

Opioid-agonist treatment: Opioid-agonist treatment consists of daily, supervised dispensing of methadone or buprenorphine, regular UDS, and counseling. Opioid-agonist treatment has been shown to be effective for treatment of prescription opioid addiction in chronic pain patients.[26] Methadone is a potent -opioid agonist with a long half-life. Buprenorphine-naloxone (Suboxone), a sublingual, partial -opioid agonist; it is safer than methadone because it has a ceiling-dose effect and is less likely to cause respiratory depression.[27] Unlike methadone, physicians do not require a special exemption to prescribe Suboxone. Controlled trials have demonstrated that buprenorphine maintenance treatment is safe and effective when prescribed in primary care settings,[28-30] and physicians should consider receiving extra training in buprenorphine prescribing if they have opioid-addicted patients in their practices.[31] Currently, provincial drug plans have only restricted coverage.

Table 6. Management of opioid misuse or addiction

PATIENT CATEGORY	MANAGEMENT
High risk of addiction (eg, past history of addiction)	• Use opioids only if first-line treatments fail • Prescribe small amounts • Perform frequent UDS • Use caution with oxycodone and hydromorphone • Keep dose well below a 200-mg/d MED
Currently addicted to other drugs (eg, alcohol)	• Opioids usually contraindicated • Refer for formal addiction treatment (methadone or buprenorphine)
Suspected opioid misuse and • has organic pain requiring opioid therapy • family physician is only source of opioids • does not inject or crush tablets • is not currently addicted to cocaine, alcohol, or other drugs	Trial of structured opioid therapy: • Dispense frequently (daily, alternate days, or twice per week) • Regular UDS (1-4 times/mo) • Pill or patch counts • Switch the patient to controlled-release preparations • Avoid parenteral use and short-acting agents • Consider switching to a different opioid, while avoiding oxycodone and hydromorphone • Taper if on dose above the 200-mg/d MED
Suspected opioid misuse and • fails or is not eligible for a structured opioid trial (eg, injecting tablets, addicted to other drugs, or acquiring opioids from other sources)	Methadone or buprenorphine treatment: • Institute daily supervised dispensing • Gradually introduce take-home doses • Frequent UDS • Provide counseling and medical care

MED—morphine equivalent dose, UDS—urine drug screening.
Reprinted from Mailis-Gagnon and Kahan.[21]

Abstinence-based treatment: Abstinence-based treatment is less effective than opioid-agonist treatment, but many patients prefer it. Family physicians can manage opioid withdrawal with clonidine or tapering doses of methadone or buprenorphine. Patients should be warned that they are at risk of overdose if they relapse to their usual opioid doses after a week or more of abstinence. Family physicians should strongly encourage patients to enter formal addiction treatment immediately following medical detoxification, as detoxification by itself is usually not successful.

Concurrent mental disorders

Patients with CNCP and psychiatric disorders are more likely to receive opioids than other CNCP patients are, and they are less likely to benefit from them.[32-34] This lower likelihood of benefit could be because they have a diminished response to opioids, an enhanced perception of pain, or both.[35-37] Cross-sectional studies have shown a higher prevalence of opioid misuse and dependence among CNCP patients with concurrent psychiatric disorders than among other CNCP patients.[33,38-40] Patients with both CNCP and mental illness are often prescribed opioids along with benzodiazepines and other sedating drugs, increasing the risk of death from intentional or accidental overdose.[41-43]

In pain patients with active psychiatric disorders, opioids should therefore be reserved for well-defined somatic or neuropathic pain conditions that have not responded to nonopioid therapy. The psychiatric condition should be treated concurrently. The opioid should be titrated slowly, with frequent dispensing and monitoring for aberrant drug-related behaviour (**Table 5**).[3,16] Particular caution is required in patients who have suicidal thoughts. The study of opioid-related overdose deaths in Ontario found that 21% of the deaths were classified as suicides.[1] Opioid tapering and discontinuation is indicated if the patient does not have improved mood or decreased pain ratings of at least 30%. In depressed patients with severe pain despite opioid therapy, comprehensive pain programs and opioid tapering are associated with improvements in both mood and pain.[44] In some cases, opioids were completely discontinued; in others the dose was substantially reduced. A trial of benzodiazepine tapering might also be considered.

Elderly patients

Opioid therapy remains underused in the elderly, despite the high prevalence of chronic pain in this population.[45-47] Clinics caring for elderly patients with well-defined pain conditions (eg, severe rheumatoid arthritis or osteoarthritis) have found very low rates of abuse and addiction.[48,49] Prescribing opioids to the elderly can be very gratifying in our experience. Even relatively low doses of weak opioids or very low doses of potent opioids can be effective (eg, 9 to 15 mg of liquid morphine per day).

Opioid use in the elderly has, however, been associated with a substantially increased risk of falls and hip fractures,[50-53] and an increased risk of delirium in elderly

patients in hospitals and nursing homes.[54] Several pharmacokinetic factors put the elderly at higher risk of opioid-induced sedation and overdose, including lower serum binding, lower stroke volume, renal dysfunction, and greater sensitivity to the psychoactive and respiratory depressant effects of opioids.[55,56] If opioids are used, they should be titrated slowly, using half the starting dose used for younger adults. In almost all cases, codeine or tramadol should be the initial agent. Opioids are contraindicated in cognitively impaired patients living alone, unless close ongoing medication supervision can be arranged. Benzodiazepines should be tapered before or during opioid initiation. The patient and family should be educated about overdose prevention (**Box 3**).[54,57]

Box 3. Reducing risk of overdose in the elderly

Use the following strategies to reduce the risk of overdose in the elderly

- Warn patients and caregivers to seek help urgently if any signs of overdose occur (sedation, nodding off, emotional lability, slow or slurred speech)
- Check with patients and families early in treatment for signs of sedation
- Monitor renal function, especially with morphine[54]
- Avoid opioids in cognitively impaired patients living alone (unless ongoing medication supervision is available)
- Initial dose in the elderly should be no more than 50% of the initial dose for younger adults
- Consider oxycodone or hydromorphone over morphine (less likely to cause sedation)[57]
- Taper and discontinue benzodiazepines
- Warn patients about the effects of alcohol use

Adolescents

Nonmedical use of opioids is common among adolescents.[58] The home is the most common source; parents with adolescent children should be advised to keep their opioid medication in a locked or inaccessible location. The risk of developing prescription drug abuse and dependence might be correlated with age of first exposure to opioids.[59] A trial of long-term opioid therapy in an adolescent should be undertaken only when he or she has a very severe somatic or neuropathic pain condition for which nonopioid alternatives have failed (eg, transverse myelitis, multiple trauma with osteomyelitis). Before initiating long-term opioid therapy, consultation and shared care should be considered with a pediatrician, an adolescent psychiatrist, or an addiction physician. The dose should be titrated slowly, with frequent dispensing and close monitoring for aberrant behaviour. If potent opioids are required, oxycodone and hydromorphone should be avoided if possible.

Pregnancy

A large case-control study found increased incidence of cardiac abnormalities in the neonates of pregnant women who had used opioids for CNCP in the first trimester.[60] Also, in a small case series, daily opioid use at therapeutic doses during pregnancy was associated with neonatal abstinence syndrome, although the clinical significance of mild neonatal abstinence syndrome is not certain.[61] In order to reduce these risks, pregnant patients or patients planning to become pregnant should have their opioids tapered and discontinued. The taper should be done slowly to avoid maternal withdrawal; acute, severe opioid withdrawal has been associated with premature labour and spontaneous abortion. If the patient experiences severe pain or pain-related disability during the taper, she can be maintained on the lowest effective dose, after reviewing the risks and benefits of continued opioid use.

Some patients rapidly convert codeine to morphine, causing neonatal toxicity during breastfeeding.[62] Therefore alternatives to codeine should be used after delivery; if codeine is prescribed, it should be given for no more than 4 days, and women should be advised to contact care providers immediately if either they or their babies show any signs of sedation. Whenever feasible, pregnant women receiving daily opioids should be referred to "high-risk pregnancy units" or physicians knowledgeable about opioid use during pregnancy. This precaution is not necessary in women who use opioids intermittently or in small doses (eg, less than a 50-mg morphine equivalent dose).

Pregnant women with suspected opioid addiction should be referred urgently to physicians who prescribe methadone. Methadone treatment during pregnancy is associated with improved obstetric and neonatal outcomes.[57,63] There is emerging evidence that buprenorphine (without the naloxone component) is also effective for opioid addiction during pregnancy.[64,65]

Conclusion

Family physicians must take into consideration the patient's age, psychiatric status, risk of addiction, and other factors when prescribing opioids for chronic pain. The risks of overdose, sedation, misuse and addiction can be minimized through strategies such as careful patient selection, slow titration, patient education, frequent dispensing, and UDS.

Dr Kahan is Associate Professor and Research Scholar in the Department of Family Medicine and Community Medicine at the University of Toronto and Medical Director of Addiction Medicine Service and a staff physician in the Department of Family Medicine at St Joseph's Health Centre in Toronto, Ont. **Dr Wilson** is Department Chair and Associate Professor in the Department of Family and Community Medicine at the University of Toronto and a staff physician in the Department of Family Medicine at St Joseph's Health Centre. **Dr Mailis-Gagnon** is Professor in the Department of Medicine, the Division of Physiatry, and the Institute of Medical Science at the University of Toronto; Director of the Comprehensive Pain Program at Toronto Western Hospital; and Chair of the ACTION Ontario Centre for the Study of Pain. **Dr Srivastava**

is Assistant Professor and Research Scholar in the Department of Family and Community Medicine at the University of Toronto and a staff physician in both the Department of Family Medicine at St Joseph's Health Centre and the Centre for Addiction and Mental Health in Toronto.

Contributors

All the authors contributed to the concept and design of the study; data gathering, analysis, and interpretation; and preparing the manuscript for submission.

Competing interests

Three of the authors were members of the core guideline research group. However, all statements in this article are the sole responsibility of the authors, and the summary was not reviewed by the National Opioid Use Guideline Group.

Correspondence

Dr Meldon Kahan, St Joseph's Health Centre, Family Medicine, 30 The Queensway, East Wing, Ground Floor, Toronto, ON M6R 1B5; telephone 416 530-6860; e-mail **kahanm@stjoe.on.ca**

References

1. Dhalla IA, Mamdani MM, Sivilotti ML, Kopp A, Qureshi O, Juurlink DN. Prescribing of opioid analgesics and related mortality before and after the introduction of long-acting oxycodone. *CMAJ* 2009;181(12):891-6. Epub 2009 Dec 7.
2. Sproule B, Brands B, Li S, Catz-Biro L. Changing patterns in opioid addiction. Characterizing users of oxycodone and other opioids. *Can Fam Physician* 2009;55(1):68-9.e1-5. Available from: **www.cfp.ca/content/55/1/68**. Accessed 2011 Sep 16.
3. National Opioid Use Guideline Group. *Canadian guideline for safe and effective use of opioids for chronic non-cancer pain.* Hamilton, ON: McMaster University; 2010. Available from: **http://nationalpaincentre.mcmaster.ca/opioid/cgop_a00_executive_summary.html**. Accessed 2011 Sep 20.
4. Kahan M, Mailis-Gagnon A, Wilson L, Srivastava A. Canadian guideline for safe and effective use of opioids for chronic noncancer pain. Clinical summary for family physicians. Part 1: general populations. *Can Fam Physician* 2011;57:1257-66 (Eng), e407-18 (Fr).
5. Fishbain DA, Cole B, Lewis J, Rosomoff HL, Rosomoff RS. What percentage of chronic nonmalignant pain patients exposed to chronic opioid analgesic therapy develop abuse/addiction and/or aberrant drug-related behaviors? A structured evidence-based review. *Pain Med* 2008;9(4):444-59.
6. Fischer B, Rehm J, Patra J. Changes in illicit opioid use across Canada. *CMAJ* 2006;175(11):1385-7.
7. Kuehn BM. Opioid prescriptions soar: increase in legitimate use as well as abuse. *JAMA* 2007;297(3):249-51.
8. Dasgupta N, Kramer ED, Zalman MA, Carino S Jr, Smith MY, Haddox JD, et al. Association between non-medical and prescriptive usage of opioids. *Drug Alcohol Depend* 2006;82(2):135-42. Epub 2005 Oct 16.
9. College of Physicians and Surgeons of Ontario. *Avoiding abuse, achieving a balance: tackling the opioid public health crisis. Opioid Project.* Toronto, ON: College of Physicians and Surgeons of Ontario; 2010. Available from: **www.cpso.on.ca/policies/positions/default.aspx?id=4324**. Accessed 2011 Sep 16.
10. Centre for Addiction and Mental Health. *Low-risk drinking guidelines*. Toronto, ON: Centre for Addiction and Mental Health; 2004.
11. Webster LR, Webster RM. Predicting aberrant behaviors in opioid-treated patients: preliminary validation of the Opioid Risk Tool. *Pain Med* 2005;6(6):432-42.
12. Turk DC, Swanson KS, Gatchel RJ. Predicting opioid misuse by chronic pain patients: a systematic review and literature synthesis. *Clin J Pain* 2008;24(6):497-508.
13. Brands B, Brands J. *Methadone maintenance: a physicians guide to treatment.* Toronto, ON: Addiction Research Foundation; 1998.
14. Manchikanti L, Manchukonda R, Damron KS, Brandon D, McManus CD, Cash K. Does adherence monitoring reduce controlled substance abuse in chronic pain patients? *Pain Physician* 2006;9(1):57-60.
15. Manchikanti L, Manchukonda R, Pampati V, Damron KS, Brandon DE, Cash KA, et al. Does random urine drug testing reduce illicit drug use in chronic pain patients receiving opioids? *Pain Physician* 2006;9(2):123-9.
16. Passik SD, Kirsh KL. Assessing aberrant drug-taking behaviors in the patient with chronic pain. *Curr Pain Headache Rep* 2004;8(4):289-94.
17. Butler SF, Benoit C, Budman SH, Fernandez KC, McCormick C, Venuti SW, et al. Development and validation of an Opioid Attractiveness Scale: a novel measure of the attractiveness of opioid products to potential abusers. *Harm Reduct J* 2006;3:5.
18. Cicero TJ, Dart RC, Inciardi JA, Woody GE, Schnoll S, Munoz A. The development of a comprehensive risk-management program for prescription opioid analgesics: researched abuse, diversion and addiction-related surveillance (RADARS). *Pain Med* 2007;8(2):157-70.
19. Zacny JP, Gutierrez S. Characterizing the subjective, psychomotor, and physiological effects of oral oxycodone in non-drug-abusing volunteers. *Psychopharmacology* (Berl) 2003;170(3):242-54. Epub 2003 Aug 29.
20. Zacny JP, Lichtor SA. Within-subject comparison of the psychopharmacological profiles of oral oxycodone and oral morphine in non-drug-abusing volunteers. *Psychopharmacology* (Berl) 2008;196(1):105-16. Epub 2007 Sep 27.
21. Mailis-Gagnon A, Kahan M. *Pocket atlas for appropriate opioid prescribing for CNCP.* Toronto, ON: Elafi; 2010.
22. Jamison RN, Ross EL, Michna E, Chen LQ, Holcomb C, Wasan AD. Substance misuse treatment for high-risk chronic pain patients on opioid therapy: a randomized trial. *Pain* 2010;150(3):390-400. Epub 2010 Mar 23.
23. Currie SR, Hodgins DC, Crabtree A, Jacobi J, Armstrong S. Outcome from integrated pain management treatment for recovering substance abusers. *J Pain* 2003;4(2):91-100.
24. Chelminski PR, Ives TJ, Felix KM, Prakken SD, Miller TM, Perhac JS, et al. A primary care, multi-disciplinary disease management program for opioid-treated patients with chronic non-cancer pain and a high burden of psychiatric comorbidity. *BMC Health Serv Res* 2005;5(1):3.
25. Wiedemer NL, Harden PS, Arndt IO, Gallagher RM. The opioid renewal clinic: a primary care, managed approach to opioid therapy in chronic pain patients at risk for substance abuse. *Pain Med* 2007;8(7):573-84.
26. Ilgen MA, Trafton JA, Humphreys K. Response to methadone maintenance treatment of opiate dependent patients with and without significant pain. *Drug Alcohol Depend* 2006;82(3):187-93. Epub 2005 Oct 10.
27. Auriacombe M, Franques P, Tignol J. Deaths attributable to methadone vs buprenorphine in France. *JAMA* 2001;285(1):45.
28. Fiellin DA, Pantalon MV, Pakes JP, O'Connor PG, Chawarski M, Schottenfeld RS. Treatment of heroin dependence with buprenorphine in primary care. *Am J Drug Alcohol Abuse* 2002;28(2):231-41.
29. Caplehorn JR. A comparison of buprenorphine treatment in clinic and primary care settings: a randomised trial. *Med J Aust* 2003;179(10):557-8.
30. Barry DT, Moore BA, Pantalon MV, Chawarski MC, Sullivan LE, O'Connor PG, et al. Patient satisfaction with primary care office-based buprenorphine/naloxone treatment. *J Gen Intern Med* 2007;22(2):242-5.
31. Kahan M, Srivastava A, Ordean A, Cirone S. Buprenorphine. New treatment of opioid addiction in primary care. *Can Fam Physician* 2011;57:281-9.
32. Sullivan MD, Edlund MJ, Steffick D, Unutzer J. Regular use of prescribed opioids: association with common psychiatric disorders. *Pain* 2005;119(1-3):95-103.
33. Sullivan MD, Edlund MJ, Zhang L, Unutzer J, Wells KB. Association between mental health disorders, problem drug use, and regular prescription opioid use. *Arch Intern Med* 2006;166(19):2087-93.
34. Breckenridge J, Clark JD. Patient characteristics associated with opioid versus nonsteroidal anti-inflammatory drug management of chronic low back pain. *J Pain* 2003;4(6):344-50.
35. Wasan AD, Davar G, Jamison R. The association between negative affect and opioid analgesia in patients with discogenic low back pain. *Pain* 2005;117(3):450-61.
36. Levenson JL, McClish DK, Dahman BA, Bovbjerg VE, de A Citero V, Penberthy LT, et al. Depression and anxiety in adults with sickle cell disease: the PiSCES project. *Psychosom Med* 2008;70(2):192-6. Epub 2007 Dec 24.
37. Riley JL 3rd, Hastie BA. Individual differences in opioid efficacy for chronic noncancer pain. *Clin J Pain* 2008;24(6):509-20.
38. Becker WC, Sullivan LE, Tetrault JM, Desai RA, Fiellin DA. Non-medical use, abuse and dependence on prescription opioids among U.S. adults: psychiatric, medical and substance use correlates. *Drug Alcohol Depend* 2008;94(1-3):38-47. Epub 2007 Dec 11.
39. Manchikanti L, Giordano J, Boswell MV, Fellows B, Manchukonda R, Pampati V. Psychological factors as predictors of opioid abuse and illicit drug use in chronic pain patients. *J Opioid Manag* 2007;3(2):89-100.
40. Wilsey BL, Fishman SM, Tsodikov A, Ogden C, Symreng I, Ernst A. Psychological comorbidities predicting prescription opioid abuse among patients in chronic pain presenting to the emergency department. *Pain Med* 2008;9(8):1107-17. Epub 2008 Feb 5.
41. Voaklander DC, Rowe BH, Dryden DM, Pahal J, Saar P, Kelly KD. Medical illness, medication use and suicide in seniors: a population-based case-control study. *J Epidemiol Community Health* 2008;62(2):138-46.
42. Cone EJ, Fant RV, Rohay JM, Caplan YH, Ballina M, Reder RF, et al. Oxycodone involvement in drug abuse deaths: a DAWN-based classification scheme applied to an oxycodone postmortem database containing over 1000 cases. *J Anal Toxicol* 2003;27(2):57-67.
43. Burns JM, Martyres RF, Clode D, Boldero JM. Overdose in young people using heroin: associations with mental health, prescription drug use and personal circumstances. *Med J Aust* 2004;181(7 Suppl):S25-8.
44. Townsend CO, Kerkvliet JL, Bruce BK, Rome JD, Hooten WM, Luedtke CA, et al. A longitudinal study of the efficacy of a comprehensive pain rehabilitation program with opioid withdrawal: comparison of treatment outcomes based on opioid use status at admission. *Pain* 2008;140(1):177-89. Epub 2008 Sep 19.
45. Moulin DE, Clark AJ, Speechley M, Morley-Forster PK. Chronic pain in Canada—prevalence, treatment, impact and the role of opioid analgesia. *Pain Res Manag* 2002;7(4):179-84.
46. Morley-Forster PK, Clark AJ, Speechley M, Moulin DE. Attitudes toward opioid use for chronic pain: a Canadian physician survey. *Pain Res Manag* 2003;8(4):189-94.
47. Solomon DH, Avorn J, Wang PS, Vaillant G, Cabral D, Mogun H, et al. Prescription opioid use among older adults with arthritis or low back pain. *Arthritis Rheum* 2006;55(1):35-41.
48. Ytterberg SR, Mahowald ML, Woods SR. Codeine and oxycodone use in patients with chronic rheumatic disease pain. *Arthritis Rheum* 1998;41(9):1603-12.
49. Mahowald ML, Singh JA, Majeski P. Opioid use by patients in an orthopedics spine clinic. *Arthritis Rheum* 2005;52(1):312-21.
50. Shorr RI, Griffin MR, Daugherty JR, Ray WA. Opioid analgesics and the risk of hip fracture in the elderly: codeine and propoxyphene. *J Gerontol* 1992;47(4):M111-5.
51. Vestergaard P, Rejnmark L, Mosekilde L. Fracture risk associated with the use of morphine and opiates. *J Intern Med* 2006;260(1):76-87.
52. Hartikainen S, Mäntyselkä P, Louhivuori-Laako K, Enlund H, Sulkava R. Concomitant use of analgesics and psychotropics in home-dwelling elderly people—Kuopio 75+ study. *Br J Clin Pharmacol* 2005;60(3):306-10.
53. Solomon DH, Rassen JA, Glynn RJ, Lee J, Levin R, Schneeweiss S. Comparative safety of analgesics in older adults with arthritis. *Arch Intern Med* 2010;170(22):1968-76. Erratum in: *Arch Intern Med* 2011;171(5):403.
54. Clegg A, Young JB. Which medications to avoid in people at risk of delirium: a systematic review. *Age Ageing* 2011;40(1):23-9. Epub 2010 Nov 9.
55. Freye E, Levy JV. [Use of opioids in the elderly—pharmacokinetic and pharmacodynamic considerations.] Article in German. *Anasthesiol Intensivmed Notfallmed Schmerzther* 2004;39(9):527-37.
56. Wilder-Smith OH. Opioid use in the elderly. *Eur J Pain* 2005;9(2):137-40.
57. Kandall SR, Doberczak TM, Jantunen M, Stein J. The methadone-maintained pregnancy. *Clin Perinatol* 1999;26(1):173-83.
58. Adlaf EM, Paglia-Boak A, Brands B. Use of OxyContin by adolescent students. *CMAJ* 2006;174(9):1303.
59. McCabe SE, West BT, Morales M, Cranford JA, Boyd CJ. Does early onset of non-medical use of prescription drugs predict subsequent prescription drug abuse and dependence? Results from a national study. *Addiction* 2007;102(12):1920-30. Epub 2007 Oct 4.
60. Broussard CS, Rasmussen SA, Reefhuis J, Friedman JM, Jann MW, Riehle-Colarusso T, et al. Maternal treatment with opioid analgesics and risks for birth defects. *Am J Obs Gyn* 2011;204(4):314.e1-11. Epub 2011 Feb 21.
61. Hadi I, da Silva O, Natale R, Boyd D, Morley-Forster PK. Opioids in the parturient with chronic nonmalignant pain: a retrospective review. *J Opioid Manag* 2006;2(1):31-4.
62. Madadi P, Shirazi F, Walter FG, Koren G. Establishing causality of CNS depression in breastfed infants following maternal codeine use. *Paediatr Drugs* 2008;10(6):399-404.
63. Kaltenbach K, Berghella V, Finnegan L. Opioid dependence during pregnancy. Effects and management. *Obstet Gynecol Clin North Am* 1998;25(1):139-51.
64. Johnson RE, Jones HE, Fischer G. Use of buprenorphine in pregnancy: patient management and effects on the neonate. *Drug Alcohol Depend* 2003;70(2 Suppl):S87-101.
65. Lacroix I, Berrebi A, Chaumerliac C, Lapeyre-Mestre M, Montastruc JL, Damase-Michel C. Buprenorphine in pregnant opioid-dependent women: first results of a prospective study. *Addiction* 2004;99(2):109-14.