Managing opioid use disorder in primary care

PEER simplified guideline

Christina Korownyk MD CCFP Danielle Perry Joey Ton PharmD Michael R. Kolber MD CCFP MSc
Scott Garrison MD CCFP PhD Betsy Thomas BScPharm G. Michael Allan MD CCFP Cheryl Bateman PSW
Raquel de Queiroz NP Dorcas Kennedy MD CCFP FCFP Wiplove Lamba MD FRCPC Dip ABAM Jazmin Marlinga MD CCFP(AM)
Tally Mogus MD CCFP(AM) Tony Nickonchuk BScPharm Eli Orrantia MD MSc CCFP FCFP Kim Reich RSW
Nick Wong MD CCFP(AM) FCFP Nicolas Dugré PharmD MSc Adrienne J. Lindblad ACPR PharmD

Abstract

Objective To use the best available evidence and principles of shared, informed decision making to develop a clinical practice guideline for a simplified approach to managing opioid use disorder (OUD) in primary care.

Methods Eleven health care and allied health professionals representing various practice settings, professions, and locations created a list of key questions relevant to the management of OUD in primary care. These questions related to the treatment setting, diagnosis, treatment, and management of comorbidities in OUD. The questions were researched by a team with expertise in evidence evaluation using a series of systematic reviews of randomized controlled trials. The Guideline Committee used the systematic reviews to create recommendations.

Recommendations Recommendations outline the role of primary care in treating patients with OUD, as well as pharmacologic and psychotherapy treatments and various prescribing practices (eg, urine drug testing and contracts). Specific recommendations could not be made for management of comorbidities in patients with OUD owing to limited evidence.

Conclusion The recommendations will help simplify the complex management of patients with OUD in primary care. They will aid clinicians and patients in making informed decisions regarding their care.

In 2017, almost 4000 opioid-related deaths occurred in Canada,[1] mostly involving illicit fentanyl or fentanyl analogues.[1] Thirty-five percent of opioid-related deaths and 53% of opioid-related hospitalizations were in people with medical opioid prescriptions.[2,3] In 2016, about 1 in 8 Canadians received an opioid prescription.[4] As little as a 5-day opioid prescription might increase the likelihood of long-term opioid use.[5,6]

Opioid use disorder (OUD) is currently defined by the *Diagnostic and Statistical Manual of Mental Disorders* (DSM), 5th edition, criteria; however, the definition has changed over time. Given this inconsistent definition and differing study designs, a reasonable estimate of OUD risk after initial opioid prescription might be 4.7%, recognizing that studies range broadly from 0% to 34%.[7-14] In response to the number of Canadians with OUD and the number of opioid-related deaths, the federal government launched a Canadian drugs and substances strategy.[15,16] In line with this strategy, national methadone prescribing restrictions were removed[17] and national OUD guidelines were published.[18]

About the same time, the PEER (Patients, Experience, Evidence, Research) group was tasked with providing a review of the OUD literature. Reassuringly, despite different evidence review processes and guideline committee membership, the resultant recommendations are similar to those found in the Canadian Research Initiative in Substance Misuse guideline.[18]

Editor's key points

- This simplified guideline for managing opioid use disorder (OUD) was developed with a primary care focus using a systematic review of systematic reviews design. Recommendations are accompanied by practice pearls and additional resources to support primary care practitioners and shared, informed decision making with patients.
- Managing patients with OUD in primary care and offering long-term opioid agonist therapy can improve patient outcomes. Adding psychosocial interventions and avoiding punitive measures might also be helpful. All discussions of treatment should involve the patient's preferences and values.
- Future randomized controlled trials should clarify the effects of pharmacologic treatments on morbidity, mortality, and social functioning (eg, employment); the management of comorbidities in OUD; and the best method of diagnosing OUD in patients taking opioids chronically.

Box 1. Recommendations summary

Primary care
- We **recommend** that management of OUD be performed in primary care* as part of the continuum of care for patients with OUD (strong recommendation, moderate-quality evidence)

Diagnosis
- Clinicians **could consider** the use of a simple tool such as the POMI if assistance is needed in identifying patients with chronic pain who might have OUD (weak recommendation, very low-quality evidence)

Pharmacotherapy
- We **recommend** clinicians discuss the use of buprenorphine-naloxone or methadone with their patients for treatment of OUD (strong recommendation, moderate-quality evidence)
  -Methadone might be superior for retention in treatment. However, buprenorphine-naloxone might be easier to implement in practice owing to fewer prescribing restrictions and considerations
- Clinicians **could consider** naltrexone for patients who have been opioid free for at least 7-10 d and who are unable or unwilling to use opioid agonist therapy (weak recommendation, low-quality evidence)
- We **recommend against** the use of cannabinoids for management of OUD (strong recommendation, very low-quality evidence)

Prescribing practices
- Clinicians **could consider** take-home doses (ie, 2-7 d) as an option when need and stability indicate (weak recommendation, very low-quality evidence)
- Clinicians **could consider** urine drug testing as part of the management of patients with OUD (weak recommendation, no RCT evidence)
- Clinicians **could consider** treatment agreements (ie, contracts) in the management of OUD for some patients (weak recommendation, no RCT evidence)
- We **recommend against** punitive measures involving opioid agonist treatment (ie, reduction in dose or loss of carries), unless safety is a concern (strong recommendation, moderate-quality evidence)

Tapering
- We **recommend against** initiation of opioid agonist treatment with the intention to discontinue in the short term. Opioid agonist treatment is intended as long-term management. Optimal duration is unknown and might be indefinite (strong recommendation, low-quality evidence)

Psychosocial
- We **recommend** the addition of counseling to pharmacotherapy in patients with OUD where available (strong recommendation, low-quality evidence)

Residential treatment
- There is **insufficient evidence** to create a recommendation for or against the use of residential treatment for patients with OUD (no recommendation, no RCT evidence)

Comorbidities
- There is **insufficient evidence** to create specific recommendations for the following comorbidities in patients with OUD: chronic pain, acute pain, insomnia, anxiety, and ADHD (no recommendation, insufficient evidence)

ADHD—attention deficit hyperactivity disorder, OUD—opioid use disorder, POMI—Prescription Opioid Misuse Index, RCT—randomized controlled trial.
*In RCTs, primary care might have included team-based care, support and training available, affiliation with substance misuse clinics, or 24-h pager support. Training and supports will vary by practitioner, practice site, and population served.

The PEER simplified guideline provides a primary care perspective and substantial adjunctive content to support primary care practitioners and shared, informed decision making with patients.

Methods

As with previous PEER guidelines,[19,20] we followed the principles of the Institute of Medicine's *Clinical Practice Guidelines We Can Trust*.[21]

Thirteen individuals, representing various practices, locations across Canada, and experience with managing OUD, made up the Guideline Committee (2 generalist family physicians [C.K., D.K.], 1 rural generalist [E.O.], 2 inner-city family physicians [J.M., T.M.], 1 addictions and pain management family physician [N.W.], 1 psychiatrist [W.L.], 1 nurse practitioner [R.Q.], 1 pharmacist [T.N.], 1 social worker [K.R.], 1 community support worker [C.B.], and 2 nonvoting pharmacist project managers [B.T., A.J.L.]). One committee member also functioned as a person with lived experience. Members disclosed all potential conflicts of interest and the full disclosure is available from **CFPlus**.* Through an iterative process, this group determined key questions to be addressed in the guideline. These questions were related to the following:

*The **full disclosure of competing interests, summarized GRADE results, the Prescription Opioid Misuse Index, a list of upcoming dosage forms for buprenorphine and naltrexone,** and **additional resources** are available at **www.cfp.ca**. Go to the full text of the article online and click on the **CFPlus** tab.

- the efficacy of primary care management of OUD;
- diagnosis of OUD;
- pharmacotherapy (buprenorphine-naloxone, methadone, naltrexone, and cannabinoids);
- prescribing practices (witnessed ingestion, urine drug testing, and treatment agreements ["contracts"]);
- tapering therapy (opioids or opioid agonist therapy [OAT]);
- psychosocial management;
- residential treatment; and
- management of comorbidities in patients with OUD (acute and chronic pain, attention deficit hyperactivity disorder, anxiety, and insomnia).

Systematic reviews were performed to answer each key question by a team of health professionals with expertise in evidence evaluation (including authors C.K., D.P., J.T., G.M.A., M.R.K., S.G., B.T., N.D., A.J.L.), with assistance from a librarian. Full details of the systematic review process are available in our copublication (**page e194**).[22] Briefly, a systematic review of systematic reviews design was chosen, with an additional randomized controlled trial (RCT) search for studies newer than the most recent systematic review. Observational studies were only used if no systematic review or RCT data were available. Two authors (D.P., J.T.) performed the search using MEDLINE, the Cochrane Library, and Google; published guidelines on OUD and reference lists of the included systematic reviews were also examined for relevant studies. Dual review and data extraction were undertaken for all reviews. Studies involving detoxification only without maintenance treatment were excluded. We used the definition of OUD as provided in individual RCTs or systematic reviews.

During this process, 2 additional questions were identified: Is there evidence to support use of OAT in the absence of usual multidisciplinary psychosocial supports? and What is the efficacy of sustained-release oral morphine in OUD? For these 2 questions, a search of PubMed was performed to identify relevant systematic reviews and RCTs.

The Guideline Committee used the results of all systematic reviews to craft practice recommendations using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology and drafted the guideline.[23] These documents were refined as needed based on consensus of the committee, as well as an extensive peer-review process involving 52 health professionals and 5 people with lived experience. As outlined by GRADE, strong recommendations were prefaced by the words "we recommend" while weak recommendations by "could consider."

Evidence limitations

There were a number of common limitations in the literature.[22] First, there is a lack of consistent terminology both in defining OUD (eg, *heroin abuse, opioid use, addiction, opioid dependency*) and in the comparators studied (eg, usual care). Most patients, particularly in treatment studies, used heroin as opposed to prescription opioids. Outcomes themselves were also measured inconsistently (eg, ongoing drug use defined by self-report, urine drug tests, or hair samples). Additionally, treatment studies suffered from high dropout rates, potentially resulting in attrition bias, and were often open label. One of the biggest concerns was the lack of patient-oriented outcomes. Most studies were not designed to determine effects on morbidity and mortality, but instead focused on drug use outcomes and surrogate markers.

Recommendations

Shared, informed decision making

While the recommendations are summarized in **Box 1**, this guideline also provides a table that outlines the relative effects of various treatments to assist with shared, informed decision making between provider and patient (**Table 1**). An algorithm and a buprenorphine-naloxone induction pathway are also provided (**Figures 1** and **2**).

Summarized GRADE results are available from **CFPlus**.* All recommendations in this guideline are meant to assist clinicians and patients in creating individualized treatment plans that incorporate patient preferences and values. Additionally, we recommend combining the evidence from this guideline with provincial regulatory requirements and standards when caring for patients with OUD. Additional resources (including links to provincial requirements) are also available from **CFPlus**.* None of the recommendations is intended for pregnant women or patients younger than 18 years of age.

Management of OUD in primary care

Four clinical trials examined OAT programs that were randomized to be either primary care based (ie, occurring in a "medical home" providing comprehensive medical care) or specialty care based (ie, in a clinic focusing on OUD).[22] Opioid-dependent patients were more likely to adhere to an OAT program (86% vs 67%), avoid street opioids (67% vs 35%), and have higher satisfaction when that program was administered by primary care.[22]

It is important to consider the supportive team environment in which the studied primary care programs were delivered. While primary care physicians were the sole prescribers, clinic-attached nurses or pharmacists were available to assist with administering the program (eg, participating in follow-up, screening urine, and administering medication). Some providers received additional education sessions or had experience with OUD, and others had access to 24-hour pager support. Patient outcomes, and the acceptability of such programs to providers, might differ if such supports are

not available. That said, in 3 randomized trials comparing OAT with placebo or waiting-list controls, OAT alone without any extra supports for patients or providers resulted in higher treatment retention (66% vs 22%, number needed to treat [NNT] of 3 at 3 to 4 months), a greater sense of well-being among patients, and lower street opioid use.[22]

We therefore recommend that, similar to other chronic diseases, management of OUD be performed in primary care as part of the continuum of care for patients with OUD.

Diagnosis of OUD

The diagnostic criteria in the DSM-IV and DSM-5 are the

Table 1. Estimated effects of treatments in opioid use disorder with GRADE rating of evidence

TOPIC	INTERVENTION VS CONTROL	OUTCOME	ESTIMATED BENEFIT, %		FOLLOW-UP RANGE	NNT OR NNH	GRADE QUALITY OF EVIDENCE
			INTERVENTION	CONTROL			
Primary care	Primary care vs specialty care	Treatment retention	86	67	12-52 wk	6	Moderate
	Primary care vs specialty care	Abstinence	53	35	12-52 wk	6	Low
Pharmacotherapy	Buprenorphine vs placebo	Treatment retention	64	39	30 d to 52 wk	4	Moderate
	Methadone vs no methadone	Treatment retention	73	22	45 d to 2 y	2	Moderate
	Methadone vs buprenorphine	Treatment retention	60	45	2-52 wk	7	Moderate
	Methadone vs buprenorphine	Abstinence	30	28	2-52 wk	NSS	Low
	Methadone vs buprenorphine	Sedation	58	26	6 wk	3	Moderate
	Naltrexone vs placebo or usual care	Treatment retention	33	25	8-26 wk	13	Low
	Naltrexone vs placebo or usual care	Abstinence	39	27	8-26 wk	9	Low
	Naltrexone vs placebo or usual care	Re-incarceration	24	33	8-40 wk	12	Low
Prescribing practices	Supervised vs unsupervised ingestion	Treatment retention	66	62	3-6 mo	NSS	Moderate
	Supervised vs unsupervised ingestion	Illicit drug use	59	53	3-6 mo	NSS	Low
Psychosocial interventions	Counseling vs minimal or no counseling	Treatment retention	74	62	16-26 wk	8	Low
	"Standard" vs extended counseling	Treatment retention	54	45	12-24 wk	NSS	Low
	Positive contingencies vs usual care	Treatment retention	75	66	6-26 wk	11	Moderate
	Medication contingencies vs usual care	Treatment retention	68	77	12-52 wk	11	Moderate

GRADE—Grading of Recommendations Assessment, Development and Evaluation; NNH—number needed to harm; NNT—number needed to treat; NSS—not statistically significant.

Figure 1

Opioid Use Disorder Primary Care Pathway

Consider Prescription Opioid Misuse Index (POMI) if patient receives prescription opioids and OUD is suspected.

Yes to ≥2 means diagnosis is more likely. If not, it is less likely.

DO YOU EVER:

- ☐ Use your medication more often, (shorten the time between doses), than prescribed?
- ☐ Use more of your medication, (take a higher doses) than prescribed?
- ☐ Need early refills for your pain medications?
- ☐ Feel high or get a buzz after using your pain medication?
- ☐ Take your pain medication because you are upset, to relieve or cope with problems other than pain?
- ☐ Go to multiple physicians / emergency room doctors, seeking more of your pain medication?

OUD
(Patient willing to start treatment and may benefit from OAT)

Buprenorphine /Naloxone
(Suboxone™)

- Patient must be in withdrawal (12-24-hours opioid-free)
- Sublingual tablet (~10 minutes to dissolve)
- Naloxone prevents IV diversion
- May be started in office or at home

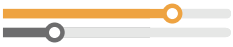
RETENTION IN TREATMENT*
64% versus **39%** with placebo
NNT‡ = 4

If one fails, consider the other.
Additional agents available.†

Methadone

- Prescribing restrictions in most provinces
- Can be started immediately
- Requires more observation and time for dose adjustment
- Liquid formulation

RETENTION IN TREATMENT
73% versus **22%** with no methadone
NNT = 2



Are psychosocial supports available?

Yes,
Offer to patient on OAT

RETENTION IN TREATMENT
74% with counselling versus **62%** no counselling
NNT = 8

No,
Opioid Agonist Therapy (OAT) alone is still effective

RETENTION IN TREATMENT
66% with OAT alone versus **22%** on wait list for OAT NNT = 3

OAT is intended for long-term management. Optimal length of therapy is unknown.

PRACTICE PEARLS

- Naloxone kits should be provided to all patients who are prescribed OAT.
- Avoid punitive measures. Continued drug use could suggest a need for treatment intensification.
- Stabilizing OUD may help with the management of chronic pain.

TREATMENT CONSIDERATIONS

Tailored to patient's needs and disease stability.

Treatment Agreement (Contract)
To outline patient and provider expectations.

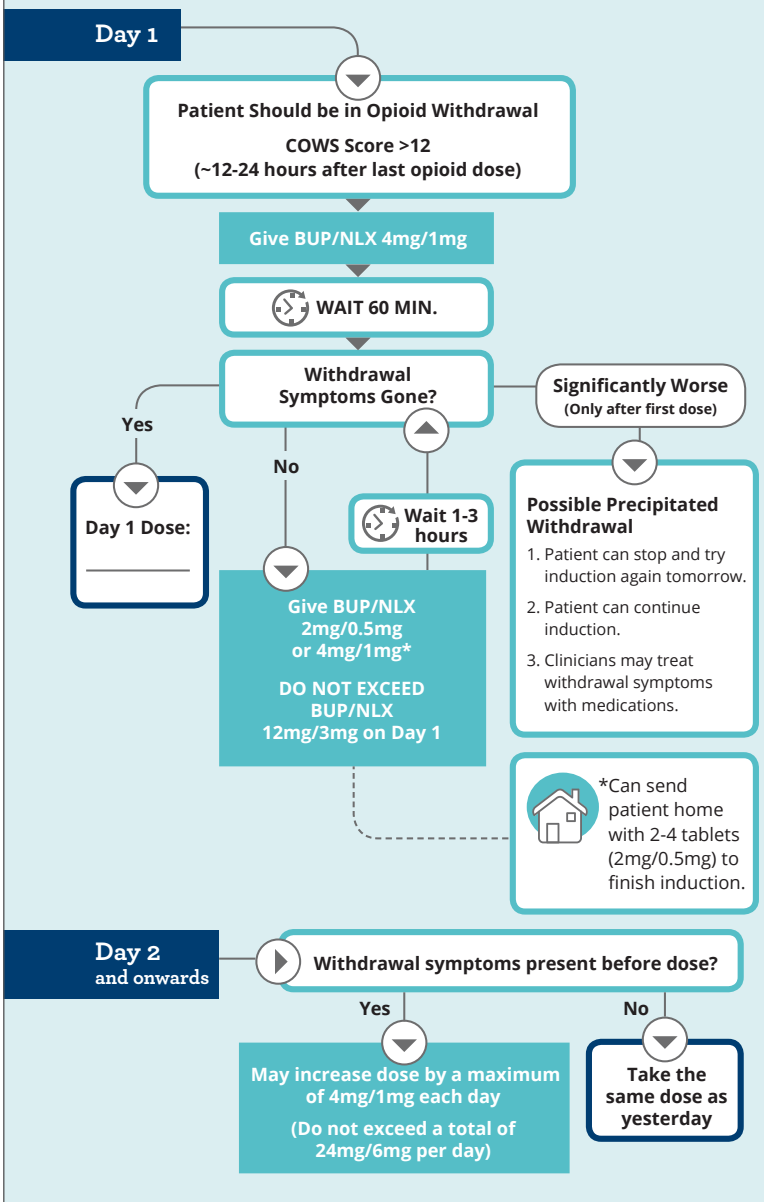
Urine Drug Testing
May be required by provincial regulations.

* Most trials report on retention in OAT treatment. While RCT data is limited on patient oriented outcomes, observational data suggests retention in treatment is associated with reduction in mortality and improvement in quality of life.
† Eg. Injectable naltrexone (opioid antagonist that requires 7-10 day opioid free period) not currently available in Canada, slow release morphine.
‡ NNT = Number Needed to Treat

Alberta College of Family Physicians

Figure 2

Buprenorphine/Naloxone (BUP/NLX) Induction Flow Diagram



Clinical Opiate Withdrawal Scale (COWS) Score (0-48)†

Category (Points), Clinician Administered

	WORSE →					
Resting Pulse Rate	0	1	2		4	
Sweating	0	1	2	3	4	
Observed Restlessness	0	1		3		5
Pupil Size	0	1	2			5
Bone or Joint Aches	0	1	2		4	
Runny Nose or Tearing	0	1	2		4	
Gastrointestinal Upset	0	1	2	3		5
Observed Tremor of Outreached Hands	0	1	2		4	
Observed Yawning	0	1	2		4	
Anxiety or Irritability	0	1	2		4	
Gooseflesh Skin	0		2	3	4	
TOTAL SCORE						

Agents for Management of Withdrawal Symptoms (Including precipitated withdrawal)

Symptom ▸ Agent	DIRECTIONS
Anxiety ▸ Clonidine	0.1mg PO Q4H PRN
Anxiety ▸ Quetiapine	25mg PO QHS PRN
Sleep ▸ Trazodone	50-100mg PO QHS PRN
Pain ▸ Ibuprofen	600mg PO Q6H PRN
Nausea ▸ Dimenhydrinate	50mg PO Q6H PRN
Nausea ▸ Ondanestron	4mg PO Q6H PRN
Diarrhea ▸ Loperamide	4mg, followed by 2mg after each loose stool (max:16mg/day)

† Full COWS Scoring Available at: https://www.drugabuse.gov/sites/default/files/files/ClinicalOpiateWithdrawalScale.pdf
For home induction, use patient administered Subjective Opiate Withdrawal Scale (SOWS) scoring available at: http://www.bccsu.ca/wp-content/uploads/2017/08/SOWS.pdf

Alberta College of Family Physicians

most accepted diagnostic criteria for OUD.[22] However, the subjectivity and length of the criteria might limit their use. We did not find any studies assessing other diagnostic criteria for OUD.

Despite finding 14 systematic reviews on identifying patients with OUD, only 2 studies compared case-finding tools with the DSM criteria.[22] The most promising tool for patients with chronic pain taking opioids is the Prescription Opioid Misuse Index (POMI), a 6-item checklist to identify patients who might have OUD (available from **CFPlus***).[24] One cohort study of 74 patients who were prescribed oxycodone for pain found that POMI scores of 2 or more points were a large help in ruling in OUD (positive likelihood ratio of 10.3) and a moderate help in ruling out OUD (negative likelihood ratio of 0.2) .[22] The COMM (Current Opioid Misuse Measure) might also be reasonable in helping diagnose OUD, but it is too long for regular use in primary care.[22] Others tools (eg, SOAPP [Screener and Opioid Assessment for Patients with Pain], ORT [Opioid Risk Tool]) have not been compared with the DSM criteria, meaning their validity in an OUD population is unknown.[22]

Based on this limited evidence, clinicians could consider the use of a simple tool such as the POMI if they require assistance identifying patients with chronic pain who might have OUD.

Pharmacotherapy

We investigated 3 main pharmacotherapies: OAT (methadone, and buprenorphine with or without naloxone) and the opioid antagonist naltrexone (a list of upcoming dosage forms is available from **CFPlus***). Although a number of RCTs have investigated the use of these drugs, none has been adequately powered to reliably report on mortality, nonfatal overdoses, suicide, hospitalizations, emergency department visits, or infectious disease transmission. However, when results from buprenorphine, methadone, and naltrexone studies are combined, a reduction in all-cause mortality is observed with the use of pharmacotherapy for OUD (odds ratio of 0.34, 95% CI 0.10 to 0.95, 7 RCTs with 1222 patients).[22]

Buprenorphine and methadone are both associated with higher rates of treatment retention than nondrug or placebo controls (buprenorphine retention is 64% vs 39% for placebo, NNT = 4, 10 RCTs; methadone retention is 73% vs 22% for controls, NNT = 2, 6 RCTs).[22] Continued opioid use is also lower with methadone (53% vs 78% for nondrug treatment or placebo, NNT = 4, 4 RCTs).[22] Continued drug use is also lower for buprenorphine, but is generally reported as the proportion of urine samples that are negative for opioids, as opposed to the proportion of patients who test negative for opioids.[22]

Indirect comparisons suggest treatment retention rates are similar for methadone and buprenorphine (73% vs 65% to 75% for buprenorphine).[22] Direct comparisons of methadone with buprenorphine, however, demonstrated higher retention with methadone (60% vs 45%, NNT = 7 at 22 weeks, 24 RCTs).[22] However, there is no difference in rates of opioid abstinence between methadone and buprenorphine (28% vs 30%, 6 RCTs) when measured via urine drug tests.[22] Adverse effects are poorly reported in RCTs. One systematic review reported more sedation with methadone than with buprenorphine based on 1 RCT (58% vs 26%, number needed to harm of 3).[22]

Naltrexone improves treatment retention (33% vs 25%, NNT=13, 8 RCTs) and decreases the risk of re-incarceration (24% vs 33%, NNT=12, 4 RCTs) compared with placebo or usual care.[22] However, naltrexone precipitates withdrawal in patients who have not undergone a 7- to 10-day opioid-free period. Because most studies were performed in patients who had already undergone detoxification (eg, incarcerated patients), the results might not be applicable to patients who are still using opioids. Data included both oral and long-acting injectable naltrexone; however, the injectable formulation is not currently available in Canada.

Sustained-release oral morphine (SROM) is another potential treatment option for OUD. Almost all RCTs were crossover trials performed in patients already stabilized on methadone. Only 1 RCT reported treatment retention in patients not taking methadone, with similar rates between methadone and SROM. High doses of SROM were required (ie, 680 mg/d). There are no RCTs of SROM in patients using opioids other than heroin.[22]

Cannabinoids are also often proposed for treatment of OUD. However, we recommend against their use owing to the absence of evidence of benefit.[22]

Overall, use of pharmacotherapy to manage OUD is strongly recommended. While methadone is superior to buprenorphine-naloxone for retention in treatment, the latter might be easier to implement in practice owing to fewer prescribing restrictions and considerations.

Prescribing practices

Some clinicians use ancillary prescribing activities (daily witnessed OAT ingestion, urine drug testing, and treatment agreements) to try to minimize the risk of medication diversion or overdose for patients with OUD. However, these activities might be time intensive and inconvenient for patients and might result in additional treatment barriers.

Daily witnessed ingestion. For most outcomes across 5 RCTs, there was no difference between "unsupervised" carries (ie, take-home doses) and "supervised" OAT ingestion.[22] However, most of the studies compared different levels of supervision (eg, comparing witnessed ingestions 2 vs 5 times per week) as opposed to unsupervised carries versus daily, supervised OAT ingestion.[22] All trials had a stabilization period (8 days to 3 months), which also might have affected outcomes.

No RCT reported on mortality or overdose rates.[22] One study reported on hospitalizations, but a typographical error rendered the findings uninterpretable.[22] The authors were contacted but were unable to clarify the error. Criminal activity was unchanged in unsupervised patients.[22] Quality of life or treatment satisfaction did not differ, but fewer patients in the unsupervised group reported diverting their medications.[22] Self-reported and urine-confirmed illicit drug use was non-significantly lower in unsupervised patients. Finally, there were no differences in treatment retention between unsupervised or supervised OAT in patients (risk ratio of 1.06, 95% CI 0.94 to 1.19).[22]

As most outcomes either found no difference or favoured unsupervised treatment, we suggest take-home doses or carries might be appropriate when need and stability indicate.

Urine drug testing. Only 1 retrospective cohort study compared the clinical outcomes of OUD patients with urine drug testing to those without; however, residual confounders might explain the differences found.[22] As a result, we can only provide a weak recommendation for using urine drug testing in managing OUD. Urine drug tests should not be used punitively. Rather, they can suggest clinical instability and possible need for treatment intensification.

Treatment agreements ("contracts"). Treatment agreements can be used to delineate expectations, negotiate boundaries, and minimize conflicts between providers and patients with OUD. One systematic review compared treatment agreements with "standard care."[22] However, only 2 of the included RCTs were in patients with OUD. These 2 studies incorporated both positive and negative contingency management (rewarding behaviour or removing privileges, respectively, based on treatment success). Unfortunately, contingencies alone can affect treatment outcomes; therefore, it is not possible to differentiate the effects of treatment agreements from contingency management in these studies.[22] Based on the principles of optimizing communication and clarifying expectations, we suggest treatment agreements be considered for some patients.

Tapering therapy

We looked at 3 definitions of tapering: tapering to discontinue prescribed opioids in patients with OUD, tapering to discontinue OAT versus continuing OAT indefinitely, and discontinuing OAT by fast versus slow tapering protocols.

Tapering to discontinue prescribed opioids in patients with OUD. We wanted to quantify the effects of tapering off prescribed opioids as a therapeutic intervention in patients with OUD. However, there are no RCTs of this approach.[22]

Tapering to discontinue OAT versus continuing OAT indefinitely. Three RCTs of tapering off OAT versus continuing OAT found that continuing OAT led to longer treatment retention and less drug use.[22] For example, in a small RCT of 12 patients, all those randomized to tapering off buprenorphine-naloxone were either unable to taper or withdrew from the study. Two other RCTs found more drug use in patients randomized to taper (eg, 0.8 more days of illicit opioid use per week).

Discontinuing OAT by fast versus slow tapering protocols. Evidence from 4 RCTs of tapering buprenorphine or buprenorphine-naloxone found that slow tapering protocols (28 to 56 days) resulted in less withdrawal symptoms and higher patient satisfaction than more rapid tapers (7 to 28 days).[22]

While tapering off OAT could be considered in some patients, OAT is intended as a long-term, potentially indefinite treatment with optimum length unknown. If considering stopping OAT, tapering should be slow and individualized to the patient.

Psychosocial interventions

The addition of standard counseling, generally defined as weekly or biweekly visits of 15 to 20 minutes' duration, significantly improves retention in treatment (74% vs 62%, NNT=8; risk ratio of 1.20, 95% CI 1.06 to 1.36) compared with very minimal or "emergency only" counseling.[22] Extended counseling (45- to 60-minute sessions weekly or biweekly) did not impart additional benefit beyond the standard intervention. Brief motivational interviewing improves treatment retention at 6 months (84% vs 73%, NNT=11).[22] Extended interventions demonstrate no additional benefit.[22] Cognitive-behavioural therapy has not been demonstrated to improve retention compared with standard care (which generally included weekly contact with the physician).[22] Thus, we recommend the addition of brief psychosocial interventions such as counseling (where available) to pharmacotherapy in patients with OUD.

Computer delivery of standard psychosocial interventions (eg, cognitive-behavioural therapy) results in similar retention outcomes to standard counseling, with reduced time commitment (264 minutes vs 647 minutes for counseling).[22] Computer-based delivery of psychosocial interventions might be an option when patients are unable or unwilling to access local resources.

One systematic review reported no benefit with the use of contingency management (using rewards and punishments for behaviour) in OUD, although all contingencies were analyzed together.[22] The use of prize and voucher (ie, positive) contingencies improves treatment retention at 12 weeks (75% vs 66%, NNT=11).[22] Reducing medication doses or removing take-home privileges for noncompliance (ie, negative contingencies) decreases treatment retention (68% vs 77%, number needed to harm

of 11) and does not reduce illicit drug use.[22] We recommend that positive reinforcement strategies be used when possible. Decreasing medication doses or revoking take-home privileges for noncompliance might be counterproductive to patient success and should be avoided unless patient or community safety is a concern.

Residential treatment

Treatments offered in residential programs can vary considerably, and some such programs prohibit the use of OAT. However, the lack of RCTs evaluating residential treatment programs prevented our creating recommendations on their use.[22]

Management of comorbid conditions in patients with OUD

Management of comorbidities in patients taking OAT can be challenging. Unfortunately, randomized controlled evidence in this area is severely lacking. With regard to the management of acute pain in patients taking OAT, 1 RCT reported morphine was superior to meperidine in an emergency setting.[22] This is not always applicable in an ambulatory setting, and nonopioid options were not explored. Similarly, the management of chronic pain in patients taking OAT remains unclear. One RCT found that all patients with chronic pain randomized to tapering off OAT dropped out of the study. A second RCT suggested that buprenorphine was not different from methadone for pain symptoms.[22] Beyond maintaining patients on OAT, the evidence does not provide adequate guidance on the issue of chronic pain.

Other examples of comorbidities that add complexity to the care of patients with OUD include insomnia, anxiety, and attention deficit hyperactivity disorder. Only 1 RCT was identified for each of these topics—all demonstrating no benefit beyond that seen with placebo.[22] While a lack of evidence limits recommendations for optimal management of these comorbidities in primary care, all patients should receive the same standard of care whether or not they have OUD.

Practice pearls

As the evidence for various aspects of managing patients with OUD is scant, the Guideline Committee created a list of practice pearls to assist clinicians in providing care for patients with OUD (**Box 2**). These pearls are based on the opinions of the committee and current trends in practice.

Box 2. Practice pearls: *Pearls are based on the opinions of the Guideline Committee and current trends in practice.*

OAT
- Promote harm reduction, such as ensuring patients have a naloxone kit
- Patients must have a lock box for take-home doses or "carries" of OAT
- Despite most references stating that the maximum dose of buprenorphine-naloxone is 24 mg/d, the dose can be increased up to 32 mg/d in select cases
- If unsure about raising the OAT dose owing to sedation concerns, ask patients to take their dose in the morning and rebook an appointment 3-4 h after the dose to ensure they are not overly sedated
- Titrate the dose of OAT based on withdrawal symptoms. Ask about the *time* of day that withdrawal symptoms are the worst. True withdrawal symptoms are worst right before the next dose is due
- Side effects of OAT are similar to those seen with opioids including constipation, amenorrhea in female patients, and low testosterone in male patients
  -Methadone can cause sweating, which can also be a withdrawal symptom
- For patients with chronic pain, first stabilize the OUD before managing pain
  -Pain outcomes might improve as OUD stabilizes
- OAT can still be used in the context of polysubstance use disorder (eg, OUD and stimulant use disorder)
- If patients are employed in safety-sensitive jobs, check employer standards for urine drug testing and pharmacotherapeutic management
- If a urine drug test result is negative for methadone or buprenorphine-naloxone (or their metabolites) in a patient taking OAT, consider the possibility of diversion

Withdrawal symptoms
- Untreated, withdrawal symptoms might last for weeks. With treatment (eg, buprenorphine), they will usually settle within 3-5 d depending on titration
- Familiarize yourself with opioid withdrawal signs and symptoms. Do the physical examination findings correlate with the patient's subjective report of symptoms?
- Craving is a withdrawal symptom

Access additional resources
- Access community pharmacists to gather information on patients you are concerned about. How do they look when they come in? Are they sedated or intoxicated?
- Consider mentorship networks, if available, to help manage comorbidities (eg, pain) or to discuss alternative management for patients with suboptimal response to OAT, etc

OAT—opioid agonist therapy, OUD—opioid use disorder.

Conclusion

Managing patients with OUD in primary care and offering long-term OAT can improve patient outcomes. Adding psychosocial interventions and avoiding punitive measures might also be helpful. All discussions of treatment should involve the patient's preferences and values. We hope that future RCTs will clarify the effects of pharmacologic treatments on morbidity, mortality, and social functioning (eg, employment); the management of comorbidities in OUD; and the best method for diagnosing OUD in patients taking opioids chronically.

Dr Korownyk is a family physician and Associate Professor in the Department of Family Medicine at the University of Alberta in Edmonton. **Ms Perry** is a nurse and Clinical Evidence Expert at the Alberta College of Family Physicians in Edmonton. **Dr Ton** is a pharmacist and Clinical Evidence Expert at the College of Family Physicians of Canada in Mississauga, Ont.

Dr Kolber is a family physician and Professor in the Department of Family Medicine at the University of Alberta. **Dr Garrison** is a family physician and Associate Professor in the Department of Family Medicine at the University of Alberta. **Ms Thomas** is a pharmacist; Project Manager, Education and Knowledge Translation at the Alberta College of Family Physicians; and Assistant Adjunct Professor in the Department of Family Medicine at the University of Alberta. **Dr Allan** is a family physician and Director of Programs and Practice Support at the College of Family Physicians of Canada and Professor in the Department of Family Medicine at the University of Alberta. **Ms Bateman** is a community support worker in Prince George, BC. **Ms de Queiroz** is a family nurse practitioner at the Referred Care Clinic in Whitehorse, YT. **Dr Kennedy** is a family physician in Lethbridge, Alta. **Dr Lamba** is a psychiatrist and addiction physician at St Michael's Hospital in Toronto, Ont. **Dr Marlinga** is a family physician at the CUPS Medical Clinic and the Family Care Clinic and a hospitalist physician at the Peter Lougheed Hospital in Calgary, Alta. **Dr Mogus** is a family physician with the Boyle McCauley Health Centre and the ARCH program of the Royal Alexandra Hospital in Edmonton and Clinical Lecturer in the Department of Family Medicine at the University of Alberta. **Mr Nickonchuk** is a clinical pharmacist at the Peace River Community Health Centre in Peace River, Alta. **Dr Orrantia** is a family physician in Marathon, Ont. **Ms Reich** is a registered social worker at the Northeast Community Health Centre in Edmonton. **Dr Wong** is a family physician with the Lifemark Chronic Pain Program in Edmonton. **Dr Dugré** is a pharmacist at the CIUSSS du Nord-de-l'Ile-de-Montréal and Clinical Associate Professor in the Faculty of Pharmacy at the University of Montreal in Quebec. **Dr Lindblad** is a pharmacist and Knowledge Translation and Evidence Coordinator at the Alberta College of Family Physicians and Associate Clinical Professor in the Department of Family Medicine at the University of Alberta.

Acknowledgment

We thank **Janice Kung,** MLIS, for her assistance with creating the search strategy; **Caitlin R. Finley, Rhonda Ting,** and **Peter (Ran) Yang** for contributing to the evidence review; our peer reviewers for their valuable feedback; and the Alberta College of Family Physicians for ongoing support. This project was funded by Alberta Health through the Primary Health Care Opioid Response Initiative.

Contributors

Drs Korownyk, Kennedy, Orrantia, Marlinga, Mogus, Wong, Lamba, Lindblad and **Ms de Queiroz, Mr Nickonchuk, Ms Reich, Ms Bateman,** and **Ms Thomas** comprised the Guideline Committee. **Drs Korownyk, Ton, Allan, Kolber, Garrison, Dugré,** and **Lindblad** and **Ms Perry** and **Ms Thomas** were part of the Evidence Review Team. All authors contributed to the recommendations and to preparing the manuscript for submission.

Competing interests

None of the authors has a financial conflict of interest to declare. The full disclosure is available from **CFPlus.***

Correspondence

Dr Christina Korownyk; e-mail **cpoag@ualberta.ca**

References

1. Special Advisory Committee on the Epidemic of Opioid Overdoses. *National report: apparent opioid-related deaths in Canada (January 2016 to March 2018).* Ottawa, ON: Public Health Agency of Canada; 2018.
2. Gomes T, Khuu W, Martins D, Tadrous M, Mamdani MM, Paterson JM, et al. Contributions of prescribed and non-prescribed opioids to opioid related deaths: population based cohort study in Ontario, Canada. *BMJ* 2018;362:k3207.
3. Gomes T, Khuu W, Craiovan D, Martins D, Hunt J, Lee K, et al. Comparing the contribution of prescribed opioids to opioid-related hospitalizations across Canada: a multi-jurisdictional cross-sectional study. *Drug Alcohol Depend* 2018;191:86-90. Epub 2018 Jul 31.
4. Canadian Institute for Health Information. *Pan-Canadian trends in the prescription of opioids, 2012 to 2016.* Ottawa, ON: Canadian Institute for Health Information; 2017. Available from: **https://secure.cihi.ca/free_products/pan-canadian-trends-opioid-prescribing-2017-en-web.pdf**. Accessed 2019 Mar 10.
5. Shah A, Hayes CJ, Martin BC. Centers for Disease Control and Prevention. Characteristics of initial prescription episodes and likelihood of long-term opioid use—United States, 2006–2015. *Morb Mortal Wkly Rep* 2017;66(10):265-9.
6. Bratt GA, Agniel D, Beam A, Yorkgitis B, Bicket M, Homer M, et al. Postsurgical prescriptions for opioid naive patients and association with overdose and misuse: retrospective cohort study. *BMJ* 2018;360:j5790.
7. Boscarino JA, Rukstalis M, Hoffman SN, Han JJ, Erlich PM, Gerhard GS, et al. Risk factors for drug dependence among out-patients on opioid therapy in a large US health-care system. *Addiction* 2010;105(10):1776-82. Epub 2010 Aug 16.
8. Sullivan MD, Edlund MJ, Fan MY, Devries A, Brennan Braden J, Martin BC. Risks for possible and probable opioid misuse among recipients of chronic opioid therapy in commercial and Medicaid insurance plans: the TROUP study. *Pain* 2010;150(2):332-9. Epub 2010 Jun 15.
9. Højsted J, Nielsen PR, Guldstrand SK, Frich L, Sjøgren P. Classification and identification of opioid addiction in chronic pain patients. *Eur J Pain* 2010;14(10):1014-20. Epub 2010 May 21.
10. Degenhardt L, Bruno R, Lintzeris N, Hall W, Nielsen S, Larance B, et al. Agreement between definitions of pharmaceutical opioid use disorders and dependence in people taking opioids for chronic non-cancer pain (POINT): a cohort study. *Lancet Psychiatry* 2015;2(4):314–22. Epub 2015 Mar 31.
11. Von Korff M, Walker RL, Saunders K, Shortreed SM, Thakrai M, Parchman M, et al. Prevalence of prescription opioid use disorder among chronic opioid therapy patients after health plan opioid dose and risk reduction initiatives. *Int J Drug Policy* 2017;46:90-8. Epub 2017 Jun 27.
12. Just JM, Bingener L, Bleckwenn M, Schnakenberg R, Wechbecker K. Risk of opioid misuse in chronic non-cancer pain in primary care patients—a cross sectional study. *BMC Fam Pract* 2018;19(1):92.
13. Higgins C, Smith BH, Matthews K. Incidence of iatrogenic opioid dependence or abuse in patients with pain who were exposed to opioid analgesic therapy: a systematic review and meta-analysis. *Br J Anaesthesia* 2018;120(6):1335-44. Epub 2018 Apr 21.
14. Minozzi S, Amato L, Davoli M. Development of dependence following treatment with opioid analgesics for pain relief: a systematic review. *Addiction* 2013;108(4):688-98. Epub 2012 Oct 18.
15. Government of Canada. *Strengthening Canada's approach to substance use issues.* Ottawa, ON: Government of Canada; 2018. Available from: **www.canada.ca/en/health-canada/services/substance-use/canadian-drugs-substances-strategy/strengthening-canada-approach-substance-use-issue.html**. Accessed 2019 Mar 10.
16. *Government of Canada actions on opioids: 2016 and 2017.* Ottawa, ON: Government of Canada; 2018. Available from: **www.canada.ca/en/health-canada/services/publications/healthy-living/actions-opioids-2016-2017.html**. Accessed 2019 Mar 10.
17. Government of Canada. *Methadone program.* Ottawa, ON: Government of Canada; 2017. Available from: **www.canada.ca/en/health-canada/services/health-concerns/controlled-substances-precursor-chemicals/exemptions/methadone-program.html**. Accessed 2019 Mar 10.
18. Bruneau J, Ahamad K, Goyer MÉ, Poulin G, Selby P, Fischer B, et al. Management of opioid use disorders: a national clinical practice guideline. *CMAJ* 2018;190:E247-57.
19. Allan GM, Lindblad AJ, Comeau A, Coppola J, Hudson B, Mannarino M, et al. Simplified lipid guidelines. Prevention and management of cardiovascular disease in primary care. *Can Fam Physician* 2015;61:857-67 (Eng), e439-50 (Fr).
20. Allan GM, Ramji J, Perry D, Ton J, Beahm NP, Crisp N, et al. Simplified guideline for prescribing medical cannabinoids in primary care. *Can Fam Physician* 2018;64:111-20 (Eng), e64-75 (Fr).
21. Greenfield S, Steinberg EP, Auerbach A, Avorn J, Galvin R, Gibbons R, et al. *Clinical practice guidelines we can trust.* Washington, DC: Institute of Medicine; 2011. Available from: **www.nationalacademies.org/hmd/Reports/2011/Clinical-Practice-Guidelines-We-Can-Trust.aspx**. Accessed 2019 Jan 19.
22. Korownyk C, Perry D, Ton J, Kolber MR, Garrison S, Thomas B, et al. Opioid use disorder in primary care. PEER umbrella systematic review of systematic reviews. *Can Fam Physician* 2019;65:e194-206.
23. Andrews J, Guyatt G, Oxman AD, Alderson P, Dahm P, Falck-Ytter Y, et al. GRADE guidelines: 14. Going from evidence to recommendations: the significance and presentation of recommendations. *J Clin Epidemiol* 2013;66(7):719-25. Epub 2013 Jan 9.
24. Cochran G, Bacci JL, Ylioja T, Hruschak V, Miller S, Seybert AL, et al. Prescription opioid use: patient characteristics and misuse in community pharmacy. *J Am Pharm Assoc* 2016;56(3):248-56. Epub 2016 Mar 24.

This article is eligible for Mainpro+ certified Self-Learning credits. To earn credits, go to **www.cfp.ca** and click on the Mainpro+ link.

This article has been peer reviewed. *Can Fam Physician* 2019;65:321-30

La traduction en français de cet article se trouve à **www.cfp.ca** dans la table des matières du numéro **de mai 2019** à la **page e173**.