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 BSPharm  G. Michael Allan MD CCFP  Cheryl Bateman PSW
Raquel de Queiroz NP  Dorcas Kennedy MD CCFP FCAP  Wiplove Lamba MD FRCP DipABAM  Jazmin Marlinga MD CCFP(AM)
Tally Mougus MD CCFP(AM)  Tony Nickonchuk BSPharm  Eli Orrantia MD MSc CCFP FCAP  Kim Reich RSW
Nick Wong MD CCFP(AM) FCAP  Nicolas Dugré PharmD MSc  Adrien 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, mostly involving illicit fentanyl or fentanyl analogues. Thirty-five percent of opioid-related deaths and 53% of opioid-related hospitalizations were in people with medical opioid prescriptions. In 2016, about 1 in 8 Canadians received an opioid prescription. As little as a 5-day opioid prescription might increase the likelihood of long-term opioid use.

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%. 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. In line with this strategy, national methadone prescribing restrictions were removed and national OUD guidelines were published.

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.

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.
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 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). 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. 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. 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). 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.\textsuperscript{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**

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

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

---

**Opioid Misuse Index (POMI)**

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?

---

**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

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

**Retention in Treatment**
- Buprenorphine/Naloxone: 64% versus 39% with placebo (NNT = 4)
- Methadone: 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.

† E.g. 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
**Buprenorphine/Naloxone (BUP/NLX) Induction Flow Diagram**

**Day 1**
- **Patient Should be in Opioid Withdrawal**
  - COWS Score >12 (~12-24 hours after last opioid dose)
  - **Give BUP/NLX 4mg/1mg**
  - **WAIT 60 MIN.**
  - **Withdrawal Symptoms Gone?**
    - Yes
      - Day 1 Dose:
    - No
      - **Wait 1-3 hours**
      - **Give BUP/NLX 2mg/0.5mg or 4mg/1mg**
      - **DO NOT EXCEED BUP/NLX 12mg/3mg on Day 1**

**Possible Precipitated Withdrawal**
1. Patient can stop and try induction again tomorrow.
2. Patient can continue induction.
3. Clinicians may treat withdrawal symptoms with medications.

**Day 2 and onwards**
- **Withdrawal symptoms present before dose?**
  - Yes
    - **May increase dose by a maximum of 4mg/1mg each day**
    - (Do not exceed a total of 24mg/6mg per day)
  - No
    - **Take the same dose as yesterday**

**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**
  - 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](https://www.drugabuse.gov/sites/default/files/files/ClinicalOpiateWithdrawalScale.pdf)
most accepted diagnostic criteria for OUD. 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. 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*). 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). 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. 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.

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).

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). Continued opioid use is also lower with methadone (53% vs 78% for nondrug treatment or placebo, NNT = 4, 4 RCTs). 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.

Indirect comparisons suggest treatment retention rates are similar for methadone and buprenorphine (73% vs 65% to 75% for buprenorphine). Direct comparisons of methadone with buprenorphine, however, demonstrated higher retention with methadone (60% vs 45%, NNT = 7 at 22 weeks, 24 RCTs).

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. 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).

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. 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.

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

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. 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. 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. One study reported on hospitalizations, but a typographical error rendered the findings uninterpretable. The authors were contacted but were unable to clarify the error. Criminal activity was unchanged in unsupervised patients. Quality of life or treatment satisfaction did not differ, but fewer patients in the unsupervised group reported diverting their medications. Self-reported and urine-confirmed illicit drug use was nonsignificantly 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).

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. 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.” 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. 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.

*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. 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 taperers (7 to 28 days).

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. 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). Extended interventions demonstrate no additional benefit. Cognitive-behavioural therapy has not been demonstrated to improve retention compared with standard care (which generally included weekly contact with the physician). 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). 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. The use of prize and voucher (ie, positive) contingencies improves treatment retention at 12 weeks (75% vs 66%, NNT = 11). 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. 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.

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. 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. 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. 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.

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.

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.

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 Clinic and a hospitalist physician at the Peter Lougheed Hospital in Calgary, Alta. Dr Mogens 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 Ortanía 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 CUSSS du Nord-de l’Île-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, Ortanía, 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 cpfplus.ca.

Correspondence

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

References


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.