PEER Simplified Guideline: Managing Opioid Use Disorder in Primary Care

ABSTRACT

Objective: To utilize 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: Twelve health professionals and a community member representing a variety of 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. They were answered by a team of professionals with expertise in literature searching and evaluation using a series of systematic reviews of randomized, controlled trials. The guideline committee used the systematic reviews to create recommendations which were peer reviewed and refined as needed before being finalized by the committee.

Recommendations: Recommendations outline the role of primary care in treating patients with OUD, as well as pharmacologic and psychotherapy treatments, and various prescribing practices (examples urine drug testing and contracts). We could not make recommendations for management of comorbidities in patients with OUD due to limited evidence.

Conclusion: The recommendations outlined here will simplify the complex management of patients with OUD in primary care. They will help clinicians and patients make informed decisions regarding their care and are not meant to dictate any particular course of action.
INTRODUCTION

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

Notwithstanding the inconsistent definition of opioid use disorder (OUD) in the literature, about 15-30% of chronic opioid users have OUD.⁷-¹² In a response to the number of Canadians with OUD and opioid related deaths, the Canadian government has launched the Canadian drugs and substances strategy.¹³,¹⁴ In line with this strategy, national methadone prescribing restrictions were removed¹⁵, and national OUD guidelines were published.¹⁶

About the same time as these guidelines were published, PEER was tasked to provide an updated 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 (CRISM) guideline.¹⁶ The PEER guideline provides a primary care perspective and substantial adjunctive content to support primary care and shared, informed decision making with patients.

METHODS

As with previous PEER created guidelines,¹⁷,¹⁸ we followed the principles of the Institute of Medicine’s Clinical Practice Guidelines We Can Trust.¹⁹

Thirteen individuals, representing a variety of practices, locations across Canada, and experience with managing OUD, made up the Guideline Committee [3 generalist family physicians (TK, DK, EO), 2 inner-city family physicians (JM, TM), 1 addictions and pain management family physician (NW), 1 psychiatrist (WL), 1 nurse practitioner (RQ), 1 pharmacist (TN), 1 social worker (KR), 1 community representative (CB) and 2 non-voting pharmacist project managers (BT and AJL)]. One committee member also functioned as a person with lived experience. Members disclosed all actual or potential conflicts of interest (Table 1). Through an iterative process, this group determined the key questions to be addressed in the guideline. These questions were related to:

1) Efficacy of primary care management of OUD
2) Diagnosis of OUD
3) Pharmacotherapy (buprenorphine, buprenorphine-naloxone, methadone, naltrexone and cannabinoids)
4) Prescribing practices (witnessed ingestion, contracts and urine drug screens)
5) Tapering therapy [opioids or opioid agonist therapy (OAT)]
6) Psychosocial management of patients on pharmacotherapy for OUD
7) Residential treatment
8) Management of comorbidities in patients on pharmacotherapy for OUD
   (acute and chronic pain, ADHD, anxiety and insomnia)

Systematic reviews were then performed to answer each key question by a team of health professionals with expertise in literature searching and evaluation (TK, DP, JT,
GMA, MK, SG, BT, CF, RT, ND, PY, AJL), with assistance from a librarian with experience with systematic reviews (JK). Full details of the systematic review process are available in our co-publication. 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/RCT data was available. Two authors (DP, JT) performed the search using Medline, Cochrane, and Google, while 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.

During this process, additional questions were identified: 1) What is the efficacy of sustained release oral morphine in OUD?, and 2) Is there evidence to support use of opioid agonist therapy (OAT) in the absence of usual multidisciplinary psychosocial supports? 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 GRADE 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 XX individuals. 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 in both defining the disorder (examples “heroin abuse”, “opioid use”, “addiction”) as well as the comparators studied (example “usual care”), which may have impacted our ability to identify studies during the search. The majority of patients, particularly in treatment studies, used heroin as opposed to prescription opioids. Outcomes themselves were also measured inconsistently (example: ongoing drug use defined by self-report, urine drug tests or hair samples). Additionally, treatment studies suffered from high drop-out rates and were often open-label. One of the biggest concerns was the lack of patient-oriented outcomes. Studies were not designed to determine effects on morbidity and mortality, but instead tended to focus on drug use outcomes and surrogate markers.

RECOMMENDATIONS

Shared, Informed Decision Making

While the recommendations are summarized in Box 1, this guideline also provides an algorithm that includes the relative effects of various treatments to assist with shared, informed decision making between provider and patient (Figure 1), as well as a flow diagram and handout for patients on initiating buprenorphine (Figure 2, Appendix XX). GRADE results are summarized in Table 2. All recommendations in this guideline are meant to assist clinicians and patients in their treatment plans, and not dictate any particular course of action. None of the recommendations are intended for pregnant women or patients under age 18.
Management of OUD in Primary Care

Four clinical trials examined OAT programs that were randomized to be either primary care-based (i.e. occurring in a “medical home” providing comprehensive medical care) or specialty care-based (i.e. take place in a clinic focusing on opioid use disorder). Opioid dependent patients were more likely to adhere to an opioid agonist therapy program (86% versus 67%), avoid street opioids (67% versus 35%), and had higher satisfaction when that program was administered by primary care.

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 and/or pharmacists were available to assist the primary care physician in administering the program (e.g. 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, may differ if such supports are not available. That said, in three randomized trials comparing to placebo or wait list control, OAT alone without any extra supports for patients or providers resulted in higher retention [66% versus 22%, Number Needed to Treat (NNT)=3 at 3-4 months], a greater sense of well-being, and lower street opioid use.

We therefore recommend that 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 Diagnostic and Statistical Manual of Mental Disorders (DSM-IV and V) is the most accepted diagnostic criteria for OUD. However, the subjectivity and length of the criteria may limit its 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 chronic pain patients on opioids is the Prescription Opioid Misuse Index (POMI), a 6-item checklist to identify patients who may have OUD. One cohort study of 74 patients prescribed oxycodone for pain found that POMI scores ≥2 points were a large help ruling-in (positive likelihood ratio 10.3) and moderate help ruling-out (negative likelihood ratio 0.2) OUD. The Current Opioid Misuse Measure (COMM) may also be reasonable in helping diagnose OUD, but is too long for regular use in primary care.

Others tools [examples the Screener and Opioid Assessment for Patients with Pain (SOAPP), or the Opioid Risk Tool (ORT)] have not been compared to the DSM, meaning their validity in an OUD population is unknown.

Based on this limited evidence, we suggest the use of a simple tool such as the Prescription Opioid Misuse Index (POMI) if clinicians require assistance identifying chronic pain patients who may have OUD.

Pharmacotherapy
We investigated three main pharmacotherapies: OATs (methadone, and buprenorphine with or without naloxone) and the opioid antagonist naltrexone (Appendix 1 lists alternative dosage forms). Although a number of RCTs have investigated the use of these drugs, none have been adequately powered to reliably report on mortality, non-fatal 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 [OR=0.29, 95%CI (0.08, 0.88), 6 RCTs].

Methadone is associated with higher rates of treatment retention than non-drug or placebo controls after 16 weeks (73% versus 22%, NNT=2, 6 RCTs). Continued opioid use is also lower with methadone (53% versus 78% non-drug treatment or placebo, NNT=4, 4 RCTs).

Indirect comparisons suggest treatment retention rates are similar for methadone and buprenorphine (73% versus 65-75% for buprenorphine). Direct comparisons of methadone to buprenorphine, however, demonstrated higher retention with methadone (60% versus 45%, NNT=7 at 22 weeks, 24 RCTs). However, there is no difference in rates of opioid abstinence between methadone and buprenorphine (28% versus 30%, 6 RCTs), when measured via urine drug screens.

Naltrexone improves treatment retention (33% versus 26%, NNT=14, 8 RCTs) and decreases the risk of re-incarceration (24% versus 33%, NNT=11, 4 RCTs) compared to placebo or usual care. However, naltrexone precipitates withdrawal in patients who have not undergone a 7-10 day opioid free period. Since most studies were performed in patients who had already undergone detoxification (example incarcerated patients), the results may not be applicable to patients who are still using opioids. Additionally, questions remain about the efficacy of oral naltrexone, and the injectable form is not available in Canada.

Sustained release oral morphine is another potential treatment option for OUD. However, the high doses used in these studies (ie. 680mg/day) likely limit its use in primary care. Cannabinoids are also often proposed for treatment of OUD. However, we strongly recommend against their use due to 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 may be easier to implement in practice due to fewer prescribing restrictions and considerations.

**Prescribing Practices**

Some clinicians use ancillary prescribing activities [witnessed daily OAT ingestion, urine drug screening and prescribing contracts] in an attempt to decrease the risk of medication diversion or overdose for patients with OUD. However, these activities may be time intensive and inconvenient to patients and may result in additional treatment barriers.

a. *Daily Witnessed Ingestion*
For most outcomes across 5 RCTs, there was no difference between ‘unsupervised’ carries (ie. take home doses) and ‘supervised’ OAT ingestion.\textsuperscript{20} This may partially be explained by the fact that most of the studies compared different levels of supervision (example comparing witnessed ingestions two versus five times per week) as opposed to unsupervised carries versus daily, supervised OAT ingestion.\textsuperscript{20} Four out of 5 trials reports some type of stabilization period (8 days to 3 months) which may have impacted outcomes as well.

No RCT reported on mortality or overdose rates.\textsuperscript{20} One study reported on hospitalizations, but a typographical error rendered their findings un-interpretable.\textsuperscript{20} Criminal activity was either unchanged or decreased slightly (11\% versus 21\%) in unsupervised patients.\textsuperscript{20} Quality of life or treatment satisfaction did not differ but fewer patients in the unsupervised group diverted their medications.\textsuperscript{20} 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 (RR 1.07; 95\% CI 0.95, 1.20).\textsuperscript{20}

Since most outcomes either found no difference or favoured unsupervised treatment, we suggest considering take-home doses or carries as opposed to daily witnessed ingestion.

\textit{b. Urine Drug Screening}

Only one retrospective cohort study compared the clinical outcomes of OUD patients with urine drug screens to those without.\textsuperscript{20} This study found all-cause mortality was reduced (HR 0.33; 95\% CI, 0.22 to 0.49) in patients who received urine drug screens compared to those who do not, regardless of the results of the test.\textsuperscript{20} However, residual confounders may explain the differences found. As a result, we can only provide a weak recommendation for using urine drug tests in managing OUD. Urine drug screens should not be used punitively, rather, they can suggest suboptimal treatment and an indication for treatment intensification if they continue to be positive for opioids.

\textit{c. Treatment Contracts}

Contracts may be used to delineate expectations, negotiate boundaries and minimize conflicts between providers and patients with OUD. One systematic review compared contracts to “standard care “ for a variety of health conditions.\textsuperscript{20} However, only 2 of the included studies were in patients with OUD. These two studies incorporated both positive and negative contingency management (rewarding behaviours 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 contracts from contingency management in these studies.\textsuperscript{20} As a result, we suggest contracts may be an option for some patients.

\textbf{Tapering Therapy}

We looked at 3 definitions of tapering.

\textit{a. Tapering to discontinue prescribed opioids in patients with OUD}
In effort to provide information for shared, informed decision making, we wanted to quantify the effects of tapering off of prescribed opioids as a therapeutic intervention in patients with OUD. However, there are no RCTs of this approach.\textsuperscript{20}

\subsection*{b. Tapering to discontinue OAT versus continuing OAT indefinitely}

A small RCT of 12 patients is the highest quality evidence that evaluates tapering off OAT to continuing long-term OAT for OUD patients.\textsuperscript{20} All patients randomized to tapering off buprenorphine-naloxone either switched to maintenance therapy or withdrew from the study completely. Another RCT found more drug use in patients randomized to taper (example 1.27 more days of illicit opioid use).\textsuperscript{20}

\subsection*{c. Discontinuing OAT by fast versus slow tapering protocols}

Evidence from 4 RCTs of tapering buprenorphine or buprenorphine-naloxone found that slow tapering protocols (28-56 days) resulted in less withdrawal symptoms and higher patient satisfaction than more rapid tapers (7-28 days).\textsuperscript{20} In summary, no RCT evidence is available to support tapering to discontinue prescription opioids in patients with OUD. While tapering off of 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, evidence suggests that tapering should be slow, over at least a 28-day period.

\section*{Psychosocial Interventions}

The addition of psychotherapy to pharmacotherapy to improve outcomes is controversial, with some groups reporting no benefit.\textsuperscript{20} We found that addition of standard counseling, generally defined as weekly or biweekly visits of 15-20 minutes duration, significantly improves retention in treatment (75\% versus 61\%, NNT=8) compared to very minimal or “emergency only” counseling.\textsuperscript{20} Extended counseling (~45-60 minute sessions weekly or biweekly) has not been demonstrated to impart additional benefit beyond the standard intervention. Brief motivational interviewing improves retention in treatment at six months (84\% versus 73\%, NNT of 11).\textsuperscript{20} Extended interventions demonstrate no additional benefit.\textsuperscript{20} Cognitive behavioural therapy has not been demonstrated to improve retention compared to standard care (which generally included weekly contact with the physician).\textsuperscript{20} Thus we recommend the addition of brief psychosocial interventions such as counseling (where available) to pharmacotherapy in patients with opioid use disorder.

The use of technology to administer known psychosocial interventions results in similar outcomes to standard counseling for retention, with less resource utilization.\textsuperscript{20} One RCT reported that those in a computer based intervention spent 264 minutes in therapy as compared to those that met with a therapist (1198 minutes) or received standard counselling (647 minutes) – with similar to better outcomes.\textsuperscript{20} We suggest clinicians consider technology based interventions based on established therapeutic tools to augment pharmacologic management of patients with opioid use disorder.

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.\textsuperscript{20} The use of prize and voucher (i.e positive) contingencies improve retention in treatment at 12 weeks (75\% versus 66\%, NNT of
Reducing medication doses or removing take home privileges for non-compliance (ie. negative contingencies), decrease treatment retention (68% versus 77%, NNH of 9) and does not reduce illicit drug use.\textsuperscript{20} We recommend that positive reinforcement strategies be used when possible. Decreasing medication doses or revoking take home privileges for non-compliance may be counterproductive to patient success and should be avoided unless patient or community safety is a concern.

\textbf{Residential Treatment}

Treatment in residential programs can vary significantly, and some prohibit the use of OAT among their clients. However, the lack of RCTs evaluating residential treatment programs prevented creating a recommendation on their use.\textsuperscript{20}

\textbf{Management of Comorbid Conditions in Patients with OUD}

Management of comorbidities in patients on OAT can be challenging. Unfortunately, randomized controlled evidence in this area is severely lacking. With regards to the management of acute pain in patients on OAT, 1 RCT reported IV morphine was superior to IV meperidine in an emergency setting.\textsuperscript{20} This is not always applicable in an ambulatory setting, and non-opioid options were not explored. Observational data reports on variations in methadone dosing and frequency for acute pain, but this has not been compared to alternate interventions.\textsuperscript{20} Similarly, the management of chronic pain in patients on OAT remains unclear. One study reported that tapering patients with chronic pain off of their OAT resulted in worse retention with all patients randomized to the taper group dropping out of the study. A second suggested that buprenorphine was not different from methadone for pain symptoms.\textsuperscript{20} However, beyond maintaining patients on OAT, the evidence does not provide adequate guidance on the issue of chronic pain.

Other examples of co-morbidities that add complexity to the care of the OUD patient include insomnia, anxiety and ADHD. Only 1 RCT was identified for each of these topics – all demonstrating no benefit beyond that seen with placebo.\textsuperscript{20} One reported no benefit of trazodone over placebo for insomnia, another reported no benefit of buspirone over placebo for anxiety, and the third reported no difference in treatment outcomes between methylphenidate, bupropion or placebo for ADHD.\textsuperscript{20} A lack of evidence for beneficial therapy options is a serious impairment to the determination of an optimal approach to management of these co-morbidities in primary care. Based on current evidence, no recommendations can be made.

\textbf{PRACTICE PEARLS}

Since the evidence for various aspects of managing patients with OUD is scant, we created a list of practice pearls to assist clinicians in providing care for patients with OUD (Box 2). These pearls are based on expert opinion and current trends in practice.

\textbf{CONCLUSION}

Management of OUD can be done in primary care, and done well. By focusing on the highest-quality evidence, this guideline tried to answer the most pressing questions
primary care clinicians face in managing OUD during the opioid epidemic. All discussions of treatment should involve the patient’s preferences and values. We hope that future randomized, controlled trials will clarify: 1) the effects of pharmacological treatments on morbidity and mortality, 2) the management of co-morbidities in OUD, and 3) the best method to diagnose OUD in patients on chronic opioids.

References


20. PEER. Umbrella systematic review of systematic reviews of opioid use disorder in primary care: setting, diagnosis, treatment, and management of co-morbidities. TBD.

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<th>Name</th>
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<th>Written Articles*</th>
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<td>Clinical Evidence Expert, Alberta College of Family Physicians</td>
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<td>Betsy Thomas</td>
<td>Pharmacist, Project Manager, Education and KT, Alberta College of Family Physicians, Assistant Adjunct Professor, Department of Family Medicine, University of Alberta</td>
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<td>Rhonda Ting</td>
<td>Pharmacist, Edmonton, Alberta</td>
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<tr>
<td>Joey Ton</td>
<td>Pharmacist, Clinical Evidence Expert, The College of Family Physicians of Canada</td>
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<tr>
<td>Peter Yang</td>
<td>BSc Pharm, MD Student, Class of 2020, University of Alberta</td>
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<td></td>
</tr>
</tbody>
</table>

* on topics related to the guidelines (opioid use disorder). ** from a commercial organization. Peer reviewers: List of peer reviewers available on request.
### Box 1. Recommendations Summary

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

**Diagnosis**
- Clinicians **could consider** the use of a simple tool such as the Prescription Opioid Misuse Index (POMI) if assistance is needed identifying chronic pain patients who may have opioid use disorder (weak recommendation, very low quality evidence).

**Pharmacotherapy**
- **We recommend** clinicians discuss use of buprenorphine-naloxone or methadone with their patients for treatment of opioid use disorder (strong recommendation, moderate quality evidence).
  - Methadone is superior for retention in treatment. However, buprenorphine-naloxone may be preferred due to potential methadone prescribing restrictions.
- Clinicians **could consider** naltrexone for patients who have been opioid free for at least 7-10 days and who are unable or unwilling to use other types of Opioid Agonist Therapy (weak recommendation, low quality evidence).
- **We recommend against** the use of cannabinoids for management of opioid use disorder (strong recommendation, very low quality evidence).

**Prescribing Practices**
- Clinicians **could consider** treatment agreements (i.e. contracts) in the management of opioid use disorder for some patients (weak recommendation, no RCT evidence).
- **We recommend against** punitive measures involving opioid agonist treatment (i.e. reduction in dose or loss of carries), unless safety is a concern (strong recommendation, low quality evidence).
- Clinicians **could consider** take-home doses (i.e. 2 to 7 days) as opposed to daily witnessed ingestion (weak recommendation, very low quality evidence).
- Clinicians **could consider** urine drug testing as part of the management of patients with opioid use disorder (weak recommendation, no RCT 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 may be indefinite (strong recommendation, very low quality evidence)

**Psychosocial**
- **We recommend** the addition of counseling to pharmacotherapy in patients with opioid use disorder 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 opioid use disorder (no recommendation, no RCT evidence).

**Comorbidities**
- There is **insufficient evidence** to create recommendations for the following co-morbidities in patients with opioid use disorder: chronic pain, acute pain, insomnia, anxiety, ADHD (no recommendation, insufficient evidence).

---

*In RCTs, primary care may have included team-based care, support/training available, affiliation with substance misuse clinic, or 24-hour pager support. Training and supports will vary per practitioner, practice site and population served.
Opioid Use Disorder
Primary Care Pathway

Probable OUD
(Patient willing to start treatment)

Buprenorphine/Naloxone
(Suboxone™)
- Patient must be in withdrawal (12-48 hours opioid-free)
- Sublingual tablet (~10 minutes to dissolve)
- Naloxone prevents IV diversion
- May be started in office or at home

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
  75% with counselling versus 61% no counselling
  NNT = 8

No
- Opioid Agonist Therapy (OAT) alone is still effective
  RETENTION IN TREATMENT
  66% versus 22% with wait list
  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 can be a sign of treatment failure.
- In patients with chronic pain and OUD, stabilize OUD before treating pain.

TREATMENT CONSIDERATIONS
- Tailored to patient’s needs and disease stability.
- Treatment Agreement (Contract)
- To outline patient and provider expectations

Urine Drug Screening
- Objective, determines treatment efficacy
- Take Home Doses (Carries)
- To reduce barriers to access

* 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.
** IM injectable Naltrexone, (opioid antagonist that requires 7-10 day opioid free period) not currently available in Canada, Slow release morphine, etc.
*** Number Needed to Treat (NNT)
Figure 2. Buprenorphine Initiation

Buprenorphine/Naloxone (BUP/NLX)
Induction Flow Diagram (Home or Office)

**Day 1**
- Patient Should be in Opioid Withdrawal COWS Score > 12
  - Give BUP/NLX 4mg/1mg
- WAIT 60 MIN.

**Withdrawal Symptoms Gone?**
- Yes
  - Day 1 Dose: ______
    - Give BUP/NLX 2mg/0.5mg or 4mg/1mg*
    - DO NOT EXCEED BUP/NLX 12mg/3mg on Day 1
  - *Can Send Patient Home to Finish Induction
- No
  - Withdrawal Symptoms Gone?
    - Yes
    - Significantly Worse
      - 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.
    - No
      - Give BUP/NLX 4mg/1mg.

**Day 2**
- If withdrawal symptoms present, take day 1 dose and an additional BUP/NLX 4mg/1mg. If not, take day 1 dose.

---

Clinical Opiate Withdrawal Scale (COWS) Score (0-48)
Category (Points), Clinician Administered

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Worst</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting Pulse Rate</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Sweating</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Observed Restlessness</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Pupil Size</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Bone or Joint Aches</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Runny Nose or Tearing</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Gastrointestinal Upset</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Observed Tremor of Outreached Hands</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Observed Tawning</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Anxiety or Irritability</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Gooseflesh Skin</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

**TOTAL SCORE**

Example of Withdrawal Symptom Management Agents

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

May Increase by 4mg/1mg per day to a maximum 24mg/6mg.
Full COWS Scoring Available at: https://www.drugabuse.gov/sites/default/files/files/ClinicalOpiateWithdrawalScale.pdf
Appendix XX. Patient Handout (will be trifold)

Subjective Opioid Withdrawal Score (SOWS)

How do you feel?
Circle each of the symptoms below from 0 to 4, based on how you are feeling right now.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Not at all</th>
<th>A little</th>
<th>Moderately</th>
<th>A lot</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td>I feel anxious.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I feel like yawning.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I am sweating.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>My eyes are teary.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>My nose is runny.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I have goosebumps.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I am shaking.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I have hot flashes.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I have cold flashes.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>My bones and muscles feel achy.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I feel restless.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I feel nauseous.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I feel like vomiting or throwing up.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>My muscles are twitching.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I have stomach cramps.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I feel like using now (craving)</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

Add up your scores for each symptom.
My SOWS score is ____.

If your score is equal to 17 or more – You are ready to start. See the inner portion of this handout.
If your score is less than 17 – Check your score again in 1 to 3 hours.
Starting Suboxone.
Suboxone is meant as a long-term treatment to help you stop and stay off opioids. Contact your healthcare provider if you have any questions following the steps to starting suboxone.

DAY ONE

Must be opioid-free for at least 12 hours and your SOWS score is 17 or higher.

You are in withdrawal. Start here.

Dissolve 4 mg (2 tabs) under your tongue for about 10 minutes.

Don't eat or drink during this time.

Medication takes about 20-45 minutes to start working.

How do you feel?
😊 I feel good. No additional doses.
😊 I still have withdrawal symptoms. Take 2 or 4 mg

Stop at 12 mg (6 tabs)

Total mg for Day 1: __

If you are feeling MUCH worse, call your physician. This could be because you started your medication before you were in withdrawal.

DAY TWO

Day Two Dose Options

Option 1: Not experiencing any withdrawal symptoms. Take total dose from day 1.

Option 2: If you are having withdrawal symptoms, add 2 mg (1 tab) or 4 mg (2 tabs) based on how bad you feel.

Stop at 16 mg (8 tabs)

Total mg for Day 2: __

DAY THREE AND ONWARD
Take total dose from previous day and add 2 mg (1 tab) or 4 mg (2 tabs) based on how bad your withdrawal symptoms feel.

The maximum total daily dose = 24 mg.
Are there ways to manage my withdrawal symptoms when I start buprenorphine-naloxone (Suboxone™)?

Your doctor may have prescribed you medications to help with your symptoms of withdrawal. These may be helpful during the first few days of starting suboxone. Once you have reached your appropriate dose of buprenorphine-naloxone, you shouldn’t need these extra medications.

Why do I have to be in withdrawal?

Starting buprenorphine-naloxone too soon will cause your withdrawal symptoms to be much worse.

Why is my physician asking me to sign a contract?

A contract is a way to talk about your goals of treating your opioid dependence. Both you and your physician can sit down and work together to make a contract that fits both of your needs and that can be modified as you progress through treatment. It is also a good way to let your doctor know your goals.

Why am I being asked to provide urine samples?

Providing urine samples can help both you and your physician track your progress and make changes to your medication.

Remember...

Keep your medicine in a safe location, locked away from children.

Have a naloxone kit with you in your home, in your vehicle and at your place of work.

Do not use drugs alone.

If you are using injectable opioids, always use clean supplies.

Access supervised consumption sites.
Table 2. Summary of GRADE Recommendations

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Strength of Recommendation</th>
<th>GRADE rating of certainty of evidence¹</th>
<th>Reasons for Downgrading/Upgrading evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>We recommend that management of opioid use disorder be performed in primary care* as part of the continuum of care for patients with opioid use disorder.</td>
<td>Strong</td>
<td>Moderate</td>
<td>Risk of imprecision (-1)</td>
</tr>
<tr>
<td>Clinicians could consider the use of a simple tool such as the Prescription Opioid Misuse Index (POMI) if assistance is needed identifying chronic pain patients who may have opioid use disorder.</td>
<td>Weak</td>
<td>Very Low</td>
<td>Risk of imprecision (-1) Risk of inconsistency (-1)</td>
</tr>
<tr>
<td>We recommend clinicians discuss use of buprenorphine-naloxone or methadone with their patients for treatment of opioid use disorder. Methadone is superior for retention in treatment. However, buprenorphine-naloxone may be preferred due to potential methadone prescribing restrictions.</td>
<td>Strong</td>
<td>Moderate</td>
<td>Buprenorphine: Risk of bias (-1) Methadone: Risk of bias (-1)</td>
</tr>
<tr>
<td>Clinicians could consider naltrexone for patients who have been opioid free for 7 to 10 days and are unable or unwilling to use Opioid Agonist Therapy.</td>
<td>Strong</td>
<td>Low</td>
<td>Risk of bias (-1) Risk of indirectness (-1)</td>
</tr>
<tr>
<td>We recommend against the use of cannabinoids for management of opioid use disorder.</td>
<td>Strong</td>
<td>Very Low</td>
<td>Risk of bias (-1) Risk of inconsistency (-1) Risk of imprecision (-1)</td>
</tr>
<tr>
<td>Clinicians could consider treatment agreements (i.e. contracts) in the management of opioid use disorder for some patients.</td>
<td>Weak</td>
<td>No RCT Evidence</td>
<td>Not Applicable</td>
</tr>
</tbody>
</table>

¹ GRADE rating of certainty of evidence includes: Low, Moderate, High.
<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Strength of Recommendation</th>
<th>GRADE rating of certainty of evidence</th>
<th>Reasons for Downgrading/Upgrading evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>We recommend against punitive measures involving opioid agonist treatment (i.e. reduction in dose or loss of carries), unless safety is a concern.</td>
<td>Strong</td>
<td>Moderate</td>
<td>Risk of bias (-1)</td>
</tr>
<tr>
<td>Clinicians could consider take-home doses (i.e. 2 to 7 days) as opposed to daily witnessed ingestion.</td>
<td>Weak</td>
<td>Very Low</td>
<td>Risk of bias (-1) Risk of indirectness (-1) Risk of imprecision (-1)</td>
</tr>
<tr>
<td>Clinicians could consider urine drug testing as part of the management of patients with opioid use disorder.</td>
<td>Weak</td>
<td>Very Low</td>
<td>Risk of imprecision (-1)</td>
</tr>
<tr>
<td>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 may be indefinite.</td>
<td>Strong</td>
<td>Low</td>
<td>Risk of bias (-1) Risk of indirectness (-1)</td>
</tr>
<tr>
<td>We recommend against tapering of opioid agonist therapy in patients recently stabilized on opioid agonist therapy and propose instead, a stable dose be reached and maintained.</td>
<td>Strong</td>
<td>Low</td>
<td>Risk of bias (-1) Risk of indirectness (-1)</td>
</tr>
<tr>
<td>We cannot recommend, for or against tapering, in patients with opioid use disorder stabilized on opioid agonist therapy long term (e.g. one year).</td>
<td>No Recommendation</td>
<td>No RCT evidence</td>
<td>Not Applicable</td>
</tr>
<tr>
<td>We cannot recommend, for or against tapering of prescription opioids in patients with opioid use disorder not on opioid agonist therapy.</td>
<td>No Recommendation</td>
<td>No RCT evidence</td>
<td>Not Applicable</td>
</tr>
<tr>
<td>Recommendation</td>
<td>Strength of Recommendation</td>
<td>GRADE rating of certainty of evidence</td>
<td>Reasons for Downgrading/Upgrading evidence</td>
</tr>
<tr>
<td>------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>------------------------------</td>
<td>--------------------------------------</td>
<td>------------------------------------------</td>
</tr>
<tr>
<td>We suggest a gradual tapering protocol: At minimum, protocols should span at least 28 days. Consider patient readiness, history, and support system Additional psychosocial services and/or adjuvant medications for withdrawal symptoms may be indicated</td>
<td>Weak</td>
<td>Low</td>
<td>Serious risk of bias (-2)</td>
</tr>
<tr>
<td>We recommend the addition of counseling to pharmacotherapy in patients with opioid use disorder where available.</td>
<td>Strong</td>
<td>Low</td>
<td>Risk of bias (-1)</td>
</tr>
<tr>
<td>Risk of indirectness (-1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>There is insufficient evidence to create a recommendation for or against the use of residential treatment for patients with opioid use disorder.</td>
<td>No recommendation</td>
<td>No RCT evidence</td>
<td>Not applicable</td>
</tr>
<tr>
<td>There is insufficient evidence to create recommendations for the following co-morbidities in patients with opioid use disorder: • chronic pain • acute pain • insomnia • anxiety • ADHD</td>
<td>No recommendation</td>
<td>Very Low</td>
<td>Risk of imprecision (-1)</td>
</tr>
<tr>
<td>Risk of indirectness (-1)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: GRADE = Grading of Recommendations Assessment, Development and Evaluation tool

*In RCTs, primary care may have included team-based care, support/training available, affiliation with substance misuse clinic, or 24-hour pager support. Training and supports will vary per practitioner, practice site and population served.
**Box 2. Practice Pearls**

**Opioid Agonist Therapy (OAT)**
- Ensure every patient on opioids or OAT has a naloxone kit.
- Patients must have a lock box for their medication.
- Buprenorphine-naloxone (Suboxone®) dose can be increased up to 32 mg/d for patients that are not adequately managed on 24 mg/d.
- If unsure about going up on OAT dose due to sedation concerns, ask patients to dose in the morning and re-book 3-4 hours post-dose to ensure they are not over sedated.
- Titrate 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.
- Methadone can cause sweating which can also be a withdrawal symptom.
- Chronic opioid therapy (from prescribed opioids, illicit opioids, or OAT) can lead to hypogonadism. Keep this in mind for patients presenting with persistent fatigue, low mood, low libido, etc.
- For chronic pain patients, first stabilize the opioid use disorder before managing pain.
- For insomnia, consider non-dependence forming substances such as melatonin or trazodone.
- OAT can still be used in the context of polysubstance use disorder (ie. OUD + stimulant use disorder).

**Withdrawal Symptoms**
- Familiarize yourself with opiate withdrawal signs/symptoms- does the physical exam 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/intoxicated?
- Consider mentorship networks if available to help manage co-morbidities (eg. pain) or to discuss alternative management for patients with suboptimal response to OAT, etc.
Appendix 2. Upcoming Drug Dosage Forms

There are a number of different dosage forms of buprenorphine and naltrexone that may become available in Canada. Some may be particularly useful for rural or remote communities due to their extended dosing intervals. Costs and insurance coverage are unknown at present.

1) Buprenorphine:
   a. Monthly injectable (Sublocade™)
   b. Subdermal 6-month implant (Probuphine™)
   c. Buprenorphine-naloxone sublingual film

2) Naltrexone:
   a. Monthly Injectable (Vivitrol™)