Opioid Agonist Therapy:
A Synthesis of Canadian Guidelines for Treating Opioid Use Disorder

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Centre for Addiction and Mental Health. *Opioid Agonist Therapy: A Synthesis of Canadian Guidelines for Treating Opioid Use Disorder*. Published May 2021. Available at www.camh.ca

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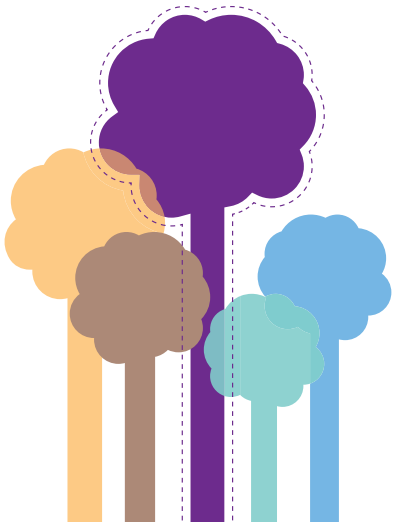

Introduction

Opioid use disorder and treatment

Opioid use disorder (OUD) is a chronic, relapsing condition that has significant personal, public health and economic consequences. Many of the fatal and non-fatal overdoses in Canada's epidemic over recent years have occurred in people with OUD. OUD may involve prescription medications (including medications that have been diverted from the medical system), or illicitly manufactured opioids, such as heroin or highly potent street fentanyl and fentanyl analogues.

People can achieve sustained long-term remission from OUD with effective treatment and follow-up. The first-line treatment for moderate to severe OUD is opioid agonist therapy (OAT), ideally combined with behavioural and social supports to optimize the determinants of health and address other psychosocial factors that influence substance use and quality of life. OAT can stabilize the cycle of intoxication and withdrawal, reduce opioid cravings and block the intoxicating effects of other short-acting opioids, including fentanyl. People who are maintained on OAT typically experience significantly improved health and social functioning and a considerable reduction in the risk of overdose and all-cause mortality.

Some people do not meet criteria for OUD, yet inject or use illicit drugs that can lead to poisonings, overdose and death. This guideline is not applicable to the management of people in these situations, and recommendations for programs and services to address their needs are beyond the scope of this guideline.

Background

Each provincial medical regulatory authority (MRA) has its own set of guidelines and standards for OAT. The aim of this unified guideline is to standardize expectations for Canadian prescribers, but not to replace any adopted guidelines; rather, this guideline was developed to complement existing initiatives and to support prescribers with best practices and evidence. It serves as a "guideline of guidelines" by synthesizing key recommendations for treating and managing OUD from existing standards, guidelines, expert opinions and best practices across Canada.

The development of this guideline was supported by the following MRAs:

- College of Physicians and Surgeons of Alberta
- College of Physicians and Surgeons of British Columbia
- College of Physicians and Surgeons of Manitoba
- College of Physicians and Surgeons of Newfoundland and Labrador
- College of Physicians and Surgeons of Ontario
- College of Physicians and Surgeons of Prince Edward Island
- College of Physicians and Surgeons of Saskatchewan

The role of the MRAs in regulating the management of OUD varies across the country. Some MRAs write clinical guidelines, provide education and have quality assurance programs that ensure safe OAT prescribing, while in other jurisdictions some of these roles are performed by independent organizations. However, what the MRAs have in common is holding registrants accountable to standards of practice. Prescribers should contact their MRA for specific guidance on this guideline and to clarify regulatory expectations for managing OUD.

Audience

The primary audience for this document is physicians who prescribe treatment for OUD. However, this guideline may be used by other health care professionals who are authorized to prescribe OAT.

Scope and process

Establishing new evidence was beyond the scope of this project. Rather, the aim was for representatives from each of the participating MRAs and independent reviewers to reach consensus regarding recommendations from existing guidelines (see the "Key opioid use disorder treatment guidelines" section). Targeted searches of peer-reviewed and grey literature were conducted in the cases of guideline discrepancies or topics with varying degrees of evidence. This document is the outcome of that process: it is a product of synthesized guidelines blended with expert opinions and evidence-based literature.

The guideline was developed using an iterative process that involved three groups: a subject matter expert group, an MRA advisory committee and an external reviewer panel. Each MRA nominated two subject matter experts and one MRA representative. The subject matter experts reviewed existing guidelines and literature and helped to develop the recommendations in this document. The MRA representatives reviewed the recommendations to ensure that they conform to regulatory standards. An external panel of clinical experts who do not have clear ties to an MRA, as well as people with lived experience, then reviewed the recommendations. The subject matter expert group considered their feedback in finalizing the recommendations.

Acknowledgment of other guidelines

Although the process of developing this document involved reviewing and synthesizing recommendations from existing guidelines, two guidelines in particular were important in developing this document: the *National Guideline for the Clinical Management of Opioid Use Disorder*, developed by the Canadian Research Initiative in Substance Misuse (CRISM), and *A Guideline for the Clinical Management of Opioid Use Disorder*, developed by the British Columbia Centre on Substance Use (BCCSU). Many of the recommendations in the current document were endorsed by clinical experts for inclusion in this guideline. Specific acknowledgments appear in sections where content has been reproduced directly from CRISM or BCCSU guidelines, or in sections where those guidelines are the only source for the recommendations in this guideline.

Structure

This document covers 26 topics divided into five parts. Part A offers guidance around harm reduction, engaging patients and initiating OAT. Part B details pharmacological treatment options. Part C presents guidance, recommendations and additional considerations to optimize outcomes in special contexts. Part D provides OAT recommendations for patients with various co-occurring disorders. Part E presents guidance on discontinuing OAT.

Each topic covers information from two perspectives:

- standards & frameworks for care (clinical targets and objectives)
- clinical recommendations for prescribers and regulated health care professionals.

Each perspective uses a chronological approach to presenting information and recommendations (i.e., the order in which the steps would likely occur in practice). Where recommendations are not suited to chronological order, they have been organized alphabetically.

Key acronyms and terms

- Bup/nlx: buprenorphine/naloxone
- BZRA: benzodiazepine receptor agonist
- CNS: central nervous system
- COWS: Clinical Opiate Withdrawal Scale
- ECG: electrocardiogram
- HIV: human immunodeficiency virus
- iOAT: injectable opioid agonist therapy
- OAT: opioid agonist therapy
- OUD: opioid use disorder
- Patient: person receiving OAT
- Prescriber: health care provider permitted to prescribe OAT
- PTSD: posttraumatic stress disorder
- QTc: corrected QT interval
- SROM: slow-release oral morphine
- Support network: defined by the patient (e.g., family, friends)
- UDT: urine drug test/testing

Additional resources

The forthcoming CAMH publication *Opioid Agonist Therapy: A Prescriber's Guide to Treatment* complements this guideline. The guideline outlines evidence-based standards and regulatory expectations (i.e., what should be done), and the guide provides further details and clinical anecdotes to help readers operationalize the guidelines (i.e., how to do it).

Disclaimer

The developers of this guideline acknowledge that there are provincial and federal legislative and regulatory contexts within which regulated health care providers operate, as well as standards they are expected to meet. The treatment and management of OUD is complex and varies due to many factors (e.g., patient health and social history, prescriber setting, availability of resources), and, as such, prescribers may encounter circumstances where these suggested guidelines are not appropriate or do not apply. This is a dynamic field and prescribers are responsible for staying up to date with emerging evidence. This guideline is not intended to be a comprehensive treatment manual or to replace good clinical judgment.

Acknowledgments

The inspiration for this document came from Wade Hillier in his role at the College of Physicians and Surgeons of Ontario (CPSO), with which the Centre for Addiction and Mental Health has an established history of collaborating to produce evidence-based publications about mental health and addiction.

In addition to acknowledging the people listed below for their involvement in this project, we also thank the people with lived experience of OUD who reviewed this guideline.

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Part A: Preparing to provide opioid agonist therapy

A1. Reducing harm

Standards & frameworks for care	Patients with OUD have same-day access to harm reduction services. A comprehensive harm reduction approach includes: ▪ outreach services ▪ access to naloxone (naloxone kit) ▪ sterile drug consumption equipment ▪ supervised consumption services ▪ education on harm reduction practices ▪ infectious disease testing ▪ access to primary care ▪ vaccinations ▪ appropriate referrals to other health and social services.
Clinical recommendations for prescribers	Routinely offer information and referral to take-home naloxone programs and other harm reduction services. Provide sterile drug consumption equipment and take-home naloxone kits on-site when possible. Offer vaccinations as appropriate. Offer pre-and post-exposure prophylaxis for HIV as indicated. Offer contraception and sexually transmitted infection prevention interventions as appropriate. Offer education and support regarding other relevant public health recommendations. Consider emerging harm reduction strategies (e.g., "safer supply") on the basis of a thorough assessment of risks related to the patient's health and quality of life, and to public safety. ▪ Safer supply should always be offered in conjunction with safety measures to mitigate risks. ▪ Until stronger evidence is available, emerging approaches should not be viewed as a standard of care.

A2. Engaging patients in treatment

Standards & frameworks for care	Care and care environments are culturally safe and appropriate, and are trauma-informed. Patients are given the option of engaging in interventions that align with their individual values and beliefs (e.g., based in community, land and culture). Patients determine their treatment goals. These goals may or may not involve abstinence from substance use, and they may extend beyond substance use outcomes. Care environments understand and reduce stigma; for example, by avoiding stigmatizing language such as “addict,” “clean” and “dirty.”
Clinical recommendations for prescribers	Reduce barriers to accessing care by: ▪ offering initial assessment and initiating treatment with minimal to no wait time ▪ creating a safe and welcoming environment ▪ removing physical access obstructions for patients with mobility impairment ▪ avoiding fees for uninsured services. Communicate evidence in ways that meet the patient’s learning needs. Offer to include the patient’s support network in discussions and decision making, and facilitate involvement when the patient agrees that it will be beneficial. Empower the patient with information and support to make choices and partner fully in treatment. Co-develop treatment approaches and plans that promote achievement of the patient’s health and quality-of-life goals, and that ensure: ▪ confidentiality ▪ cultural safety and appropriateness ▪ developmental appropriateness ▪ goal-orientation with an understanding of patient priorities ▪ freedom from judgment ▪ person-centredness ▪ trauma-informed care ▪ adaptability for changes in the patient’s goals and preferences. Establish indicators for measuring progress toward the patient’s goals and jointly establish a plan for revisiting the treatment approach based on the patient’s experience and perspective, and on clinical observations.

A3. Building relationships with patients and other health care and service providers

Standards & frameworks for care	Patients with OUD have comprehensive assessments and care plans that are developed in collaboration with and shared with other care providers (e.g., family physician, nurse practitioner, pharmacist). Patients receive integrated, concurrent and culturally safe management of their: ▪ physical health ▪ mental health ▪ additional addiction treatment needs ▪ needs related to social determinants of health. Ancillary service providers (e.g., public insurance plans, community housing resources, income support programs) recognize the adverse outcomes of untreated OUD and facilitate stable social environments and access to resources to promote retention in treatment.
Clinical recommendations for prescribers	Identify patients at risk of OUD and ask about opioid use (prescribed, non-prescribed and illicit) and use of other prescribed and over-the-counter medications; assess further as appropriate. Ask questions to understand the patient's health history and goals. Use that information to identify interventions that address needs consistent with the patient's clinical situation, values and goals. Incorporate the principles of trauma-informed practice, including: ▪ trauma awareness ▪ choice, collaboration and connection ▪ safety and trustworthiness ▪ skill building ▪ strengths-based approaches. Facilitate access to services that address the patient's physical and mental health needs, additional addiction treatment needs and needs related to social determinants of health. If these are not available on-site, offer referrals as appropriate for: ▪ housing ▪ income supports ▪ family supports (e.g., for postpartum needs) ▪ legal aid ▪ drug coverage ▪ peer support groups ▪ vocational and skills training ▪ cultural supports. Routinely offer psychosocial interventions and supports in conjunction with pharmacological treatment of OUD.

Clinical recommendations for prescribers	Regularly monitor clinical stability, as determined by patient characteristics that include: ▪ improved quality of life (including self-rated quality of life) ▪ improved psychiatric symptoms ▪ reduced exposure to health and social hazards ▪ progress toward substance use goals ▪ improvements in social determinants of health (e.g., housing; employment; relationships, including increased engagement with health services).

A4. Expectations for prescribers of opioid agonist therapy

Standards & frameworks for care	Prescribers stay current on literature, guidelines and best practices to provide a comprehensive range of accessible, evidence-based and trauma-informed treatments and care. Prescribers seek professional development opportunities that focus on: ▪ inclusion, diversity and equity ▪ intergenerational trauma ▪ individual, family and community healing from trauma.
Clinical recommendations for prescribers	Engage in continuing professional development to maintain and improve competence in assessing and treating substance use disorders and prescribing OAT. Establish an ongoing direct relationship with a colleague or collegial group with experience and expertise in treating OUD. Include multiple disciplines in the patient's team of care providers, depending on the needs identified in the treatment plan; for example: ▪ other physician specialists ▪ addiction counsellor ▪ social worker ▪ pharmacist ▪ care coordinator ▪ peer support worker. Establish a contingency plan with the patient for continuity of care in the event of your absence or closure of practice that meets the reasonable expectations of the patient and the needs identified in the treatment plan.

A5. Initiating opioid agonist therapy

Standards & frameworks for care	Patients with OUD have access to OAT within 48 hours. Patients with OUD have access to OAT in various settings. Hospitalization and incarceration are used as opportunities for patients who meet criteria for OAT to be initiated on this treatment.
Clinical recommendations for prescribers	Conduct a comprehensive assessment and ensure that you have reviewed and documented the following: ▪ medical history (e.g., cardiovascular health, details about chronic or recurrent pain) ▪ appropriate physical examination with laboratory testing (e.g., skin and cardiovascular exam, urine drug testing, pregnancy, HIV, hepatitis B & C) and baseline ECG ▪ pattern of substance use (including nicotine and alcohol) ▪ addiction treatment history and response ▪ psychiatric history and mental health (current and past, including suicidal ideation and attempts) ▪ health hazards that increase the risk of severe adverse events (e.g., using alone, injection use, limited access to safer injecting practices, overdose history, illicit supply, limited access to emergency care) ▪ social hazards that increase the risk of severe adverse events (e.g., violent victimization, sex work, involvement in crime, social exclusion, safety-sensitive work, risk of child apprehension) ▪ access to social supports, including income sources, drug coverage, health care coverage (awareness of coverage is especially important when considering newer buprenorphine products or slow-release oral morphine). Communicate with the patient before initiating OAT: ▪ Establish that the patient meets criteria for moderate to severe OUD, as outlined in the *Diagnostic and Statistical Manual of Mental Disorders*. ▪ Ensure that there has been a documented discussion about the benefits, risks and side effects of OAT, and duration of treatment. ▪ Educate the patient about safely storing and disposing of medication to prevent accidental poisoning by children, pets and the public. ▪ Ensure that the patient understands what is expected of the care team, with emphasis on the patient's right to non-judgmental treatment and recourse if they experience stigma and discrimination. ▪ Obtain full informed consent from the patient. ▪ Document treatment goals and plans in a signed treatment agreement to be shared with the dispensing pharmacy. Conduct an abbreviated assessment to expedite initiation of OAT if scheduling a full assessment may delay treatment in a patient at risk of severe adverse outcomes of opioid use. A full assessment with treatment planning should follow within one to two weeks. In patients who only meet criteria for mild OUD, weigh the risks of potentially long-term OAT against potential short- and long-term benefits. Such decisions should be made jointly with the patient, and documented.

A6. Effective use of ECGs

Standards & frameworks for care	Lack of access to ECGs is not a barrier to receiving OAT. If ECGs are not readily available, prescribers use clinical judgment to guide decisions about initiating OAT.
Clinical recommendations for prescribers	Obtain an ECG before initiating OAT (whenever possible) to measure the QTc interval, and document when the ECG requisition was provided. Consider obtaining ECGs when additional QTc monitoring is warranted. Take into account the following conditions when deciding whether to obtain additional ECGs and how frequently to conduct them: ▪ family history of prolonged QTc or sudden death ▪ patient has had previous arrhythmias/hospitalizations (e.g., Torsades de Pointes syndrome) ▪ patient has unexplained symptoms that suggest cardiac involvement (e.g., syncope, presyncope, palpitations, seizure activity, blurred vision without other explanations) or a predisposition to poor cardiac health ▪ patient is initiated on (or already takes) medications known to prolong the QTc interval ▪ patient is using illicit substances known to prolong the QTc interval (e.g., cocaine, crystal methamphetamine) ▪ patient develops a medical condition that increases the risk of QT prolongation (e.g., excessive vomiting) ▪ methadone dose meets or exceeds 120 mg. Collaborate with the pharmacist and use pharmaceutical information records regularly to monitor patients on medications known to prolong the QTc interval. Review the potential risks and benefits with patients if the QTc interval is higher than 450 msec but less than 500 msec. Monitor more frequently with ECGs and consider dose reductions, with close monitoring for relapse. Consider the risks and benefits of continued treatment at the current dose of methadone if the QTc interval exceeds 500 msec. Do the following if the QTc is elevated: ▪ Review medication profile to check for other QT-prolonging medication. ▪ Discuss alternative agonist therapies (buprenorphine products, slow-release oral morphine). ▪ Check and manage electrolyte abnormalities (including hypokalemia, hypomagnesemia, hypocalcemia). ▪ Consult a cardiologist. Collaborate with other prescribers and pharmacists to mitigate arrhythmia risk in patients with concerning QTc intervals. Recognize that the probability of mortality from non-retention on OAT in a patient who does not wish to change treatment options may exceed the mortality risk presented by an elevated QTc interval.

A7. Effective use of urine drug testing

Standards & frameworks for care	Urine drug testing (UDT) is not used punitively; rather, it is used as one tool in a comprehensive risk assessment to provide information about exposures and risks, promote patient safety, guide care decisions such as adequacy of dose, and monitor progress toward treatment goals. Overuse of UDT may exacerbate stigma and increase service costs. How UDT can be applied to assessment depends on: ▪ context (e.g., unpredictability of illicit drug market, difficulty in providing a substance use history) ▪ risks (e.g., engagement in safety-sensitive tasks, challenges with multiple CNS depressants) ▪ goals (e.g., engagement in positive reinforcement / contingency management programs, goal of abstinence for which UDT results motivate progress).
Clinical recommendations for prescribers	Conduct UDT when there is a clear plan for how results will benefit the patient and in ways that help to characterize risks and rationalize interventions, at times such as: ▪ when initiating OAT ▪ when adjusting doses during stabilization ▪ when there is concern about a patient's presentation ▪ when the patient requests UDT. Be mindful that the purpose of UDT is not to "catch a patient lying," but to provide information to help assess and manage risks and guide treatment decisions between clinician and patient. Assess substance use weekly while stabilizing the patient on OAT; this may involve UDT if clinical assessment, including history, requires supplementary lab investigations. Conduct UDT every one to three months in a patient with stable OUD on OAT. If unscheduled UDT would impose a net quality-of-life disadvantage (e.g., by interfering with employment or beneficial social engagement), consider scheduled UDT or combining UDT with physician/counselling appointments. ▪ Occasional unscheduled UDT may be helpful to identify medication non-adherence or concomitant use of substances with short elimination half-lives that may not be detected in scheduled testing. Use clinical judgment and consider the usefulness of history/observation in assessing progress, as well as patient preferences and individual circumstances, when determining the frequency of UDT. Counsel patients who do not attend UDT within 24 to 48 hours of a request for specimen collection about the value of UDT to the treatment plan, and take measures to facilitate testing if there are barriers.

Clinical recommendations for prescribers	Avoid taking a punitive approach if a patient provides a tampered specimen. Seek to understand the patient's concerns about UDT, and explore ways to help them feel comfortable discussing substance use and to make UDT useful to both patient and clinician. If UDT is used in the context of a contingency management strategy, emphasize positive reinforcement, such as enhancing flexibility in treatment, to help the patient achieve abstinence or quality-of-life goals. Conduct UDT to help you assess the appropriateness of take-home doses. If test results are consistent with self-report and you determine that the benefits to quality of life and social engagement outweigh the risks of diversion or overdose, consider take-home doses. Reduce take-home doses if the overall assessment indicates that the risk to the patient or community is greater than any benefit of take-home doses. Couple this approach with compassionate motivational counselling. Document UDT results, taking into account the test's relevance and importance to assessment and treatment monitoring, and indicating clinical actions that arise from results in combination with other clinical observations. Recognize that both laboratory testing and point-of-care immunoassays are useful clinical tools for monitoring OAT safety and effectiveness. The UDT modality used should be justified based on: ▪ clinical indication (e.g., urgency of clinical decision making around prescribing safety or immediate safety of take-home dosing) ▪ legal indications (monitoring for workplaces or child custody) ▪ availability of resources, especially in regions where laboratory access and capacities are limited ▪ cost. Ideally, request that urine specimens are tested using mass spectrometry or chromatography assays by a qualified laboratory because point-of-care testing has limitations due to high risk of error and false negatives. If point-of-care immunoassays are used: ▪ Use only tests approved by Health Canada, and always according to the product monograph. ▪ Understand the sensitivity, specificity, positive and negative predictive values and limitations of the test (e.g., opioid results may be negative when fentanyl has been ingested; cannabinoid results may be negative when synthetic cannabinoids have been used). Use laboratory testing with mass spectrometry and liquid chromatography to detect the following substances: ▪ specific synthetic and semisynthetic opioids (oxycodone, hydromorphone, heroin, fentanyl, newer fentanyl analogues) (some point-of-care tests can now detect fentanyl) ▪ types of sedative hypnotics (designer benzodiazepines such as etimazole) ▪ synthetic cannabinoids (e.g., Spice).

Clinical recommendations for prescribers	Consider using laboratory testing with mass spectrometry and liquid chromatography to confirm unexpected test results of immunoassays. For example, some medications and substances can cause false-positive immunoassay results (e.g., quinolones, rifampin, imipramine, dextromethorphan). Recognize that different screening tests may be required to detect alcohol use. Point-of-care breathylzers can guide safe OAT dose administration in patients who may have been drinking very recently. To detect alcohol use for monitoring purposes, specific tests may be ordered (e.g., ethyl glucuronide, ethyl sulfate, carbohydrate deficient transferrin). Recognize that UDT results are intended for therapeutic use only and should not be shared with other agencies for non-medical reasons, such as providing evidence for legal purposes (e.g., child–family services, prosecutors). ▪ An appropriate response to an agency could be to write an advocacy letter on behalf of the patient. This letter can describe the patient's clinical stability and make a general statement about the patient's participation in regular UDT for therapeutic purposes. ▪ Patients who request that their UDT results be shared with outside agencies should be advised about the possible unintended consequences of sharing this information.

A8. Providing prescriptions for opioid agonist therapy

Standards & frameworks for care	A secure and accessible modality, in accordance with federal and provincial regulations, is used to ensure the transmission of the correct prescription to the correct pharmacy in a safe and timely manner. Prescribers avoid financial conflicts of interest when choosing medications, pharmacies and dispensing schedules.
Clinical recommendations for prescribers	Communicate with the pharmacist before initiating a prescription: ▪ Assess whether the pharmacy is the most appropriate option for the patient, considering various factors and based on availability in the region (e.g., open daily, accepting new patients, geographically accessible, experienced in OUD treatment, able to provide harm reduction resources). ▪ Discuss the patient's current health status and treatment plan. ▪ Agree on suitable ways to share information about the patient's progress (including management of lost or missed doses). ▪ Establish processes for urgent communication (e.g., on-call system, after-hours contacts). ▪ Be aware of current or potential medication shortages and work with the pharmacist to mitigate any risks or impact for the patient.

Clinical recommendations for prescribers	Write prescriptions that are tamper-proof and that indicate the following: ▪ date when the prescription was written ▪ drug name and dose (mg dose in both words and numbers, as well as *total* milligram amount in words and numbers, is required by some medical regulatory authorities) ▪ start and end date stated as inclusive ▪ dosing regimen, including observed and take-home dose days ▪ induction dosing schedule with clear instructions ▪ special instructions and extraordinary situations. Before issuing a new prescription (e.g., when changing doses), verify that the patient is able to obtain the new prescription; then cancel any active and outstanding prescriptions to prevent medical/pharmacy error. Recognize that printed prescriptions have inherent risk and that e-prescribing can reduce lost prescriptions, duplication and diversion. E-prescribing also facilitates communication between prescriber and pharmacist about medication adherence. Understand, however, that e-prescribing can also carry risks (e.g., technology-related issues, including network security issues; reduced patient engagement), and take steps to mitigate them.

Part B: Providing different forms of opioid agonist therapy

B1. Choosing a pharmacological treatment

Standards & frameworks for care	A prior trial of non-pharmacotherapy or abstinence-based approaches is not a prerequisite for choosing OAT. Buprenorphine/naloxone (bup/nlx) is rapidly available as the first-line treatment for patients with OUD. It is recognized that for many patients any OAT carries a substantially lower risk of adverse events than no OAT. Evidence-based OAT options are exhausted before other options are explored. Alternative pharmacological treatments are approached with caution, and the rationale, including risk-mitigation strategies, is thoroughly documented (e.g., observed dosing, safe storage, overdose prevention).
Clinical recommendations for prescribers	Avoid withdrawal management as a stand-alone treatment for OUD because this option is not effective or safe. Ensure before initiating OAT that there has been a documented discussion with the patient about potential issues, side effects, risks, duration of treatment, and difficulty withdrawing and tapering. Consider treatment intensity when determining the most appropriate OAT option. Adjust the intensity to accommodate the changing circumstances and preferences of the patient. Initiate OAT with bup/nlx whenever it is assessed to carry a lower risk than other agonist therapies because of its pharmacologic characteristics and the advantages of more flexible take-home dosing. Consider long-acting preparations of buprenorphine (monthly injections or six-month subdermal implants) when appropriate to facilitate reintegration into society and reduce health care burden. Initiate OAT with methadone when treatment with bup/nlx is not preferable (e.g., intolerance, patient preference, challenging induction, inadequate response to bup/nlx).

Clinical recommendations for prescribers

Recognize that some patients who show a successful and sustained response to methadone may wish to transition to bup/nlx. This is an option for patients who:

- request more treatment flexibility with increased take-home doses
- are seeing a better side-effect and drug-interaction profile
- wish to withdraw from OAT but have difficulty tapering off methadone and might better tolerate a taper from bup/nlx.

The decision to transition to bup/nlx must be balanced with potential risks of destabilization, which may increase when transitioning from higher methadone doses. Options to mitigate risk include slowly reducing methadone before making the transition, microdosing bup/nlx or switching to slow-release oral morphine (SROM) for five days after stopping methadone and before initiating bup/nlx.

Consider SROM only when bup/nlx and methadone are ineffective, contraindicated or refused.

- If considering SROM in exceptional cases where bup/nlx and methadone have not been tried, conduct a thorough risk assessment and, taking into consideration your experience and the complexity of the case, consult at least one colleague with extensive experience in treating severe OUD.
- Conduct a thorough risk assessment if considering SROM in adolescents and older adults because there is little evidence for using SROM in people with a relatively short duration of OUD and because older adults may be susceptible to adverse events due to complicating medical conditions or drug interactions. Also consult a pharmacist when needed.
  - The assessment should cover exposure and susceptibility factors that may increase risk of severe adverse events, as well as risks to patient health and safety if not retained on agonist therapy.

Recognize that in patients and communities with high rates of illicit fentanyl use, emerging practices include combining methadone and SROM to allow for adequate dosing to meet high levels of tolerance. Some guidance is emerging based on clinical experience, but no clinical trials have been published to date to inform definitive practice guidelines.

Consider supervised injectable OAT (iOAT) (with diacetylmorphine or hydromorphone) if an appropriate, typically government-funded program is available for patients who both:

- continue to inject drugs despite adequate trials of non-injection agonist therapies (or are not retained on these treatments)
- continue to experience severe medical and social consequences due to continued injection drug use (e.g., overdose, infection, trauma, homelessness).

Use thorough risk assessment, documentation and consultation if you choose to depart from recommended guidelines or explore areas of medicine that are less developed. If established practice and quality standards do not yet exist, consider available randomized controlled trials, evidence-based research or consensus protocols and general best practices.

B2. Prescribing buprenorphine/naloxone

Standards & frameworks for care	Prescribers are equipped with the skills and knowledge to manage patients who are prescribed bup/nlx and to collaborate with members of the patient's interprofessional health care team.
Clinical recommendations for prescribers	**Induction phase** Prescribe 2−4 mg of bup/nlx as an initial supervised dose when the patient is in moderate to severe withdrawal (COWS ≥ 13). Up to 6 mg is acceptable in clinically required situations, but may increase the risk of precipitating withdrawal. Reassess the patient after one to three hours and prescribe additional observed doses if necessary (e.g., COWS > 8, symptoms of withdrawal). ▪ Be careful not to precipitate withdrawal by giving too high a dose or by medicating in the absence of observable withdrawal. ▪ One or two 2 mg tablets to take home may be provided if repeated observation is not feasible in the clinical setting, with clear instructions on timing the dose to avoid precipitating withdrawal. Avoid prescribing more than 12 mg total on the first day. Consider alternative induction approaches such as: ▪ "microdosing," starting with 0.5 mg twice per day, with increasing doses to a total daily dosage of 12 mg over 5–7 days for patients who cannot tolerate the significant period of abstinence needed to start bup/nlx with a conventional induction ▪ "rapid microdosing," administering 0.5–1 mg at shorter intervals, up to 12 mg total in a 24-hour period. **Titration and stabilization phase** Titrate based on withdrawal symptoms and side effects until an optimal dose has been reached, typically on day 3. Doses may be doubled every day, up to a maximum of 24 mg on day 3. Consider an alternative approach: add up the dose given on day 1 and administer it as the first dose of day 2, followed by additional doses based on the re-emergence of withdrawal symptoms. On day 3, add up the doses administered on day 2 and provide additional doses as necessary. Repeat daily until the patient is stable (no withdrawal, or COWS scores < 8 for 24 hours) or until a maximum of 24 mg per day is achieved. Use slow titration with older adults, patients taking other CNS depressants and patients with questionable opioid tolerance, balancing the risk of lower treatment retention with the risk of over-sedation: ▪ Increase bup/nlx by 2−6 mg per day until an optimal dose has been reached (24 hours of no withdrawal symptoms, extinction of cravings to use opioids, absence of toxicity).

Clinical recommendations for prescribers

Arrange for the patient to be seen by a member of the health care team to assess effectiveness and safety (e.g., excess sedation). Base reassessment frequency on the intensity of induction.

Maintenance phase

Use clinical judgment to maintain an optimal individualized daily dose, which is up to a maximum of 24 mg per day.

- If exceeding 24 mg in exceptional circumstances, inform the patient that this is a departure from approved doses and that there is limited evidence of a benefit with doses higher than 24 mg (and possibly an increased risk of adverse events).
- Review the case with an experienced colleague before trialing a dose higher than 24 mg per day and attempt to reduce the dose to approved levels (as tolerated) once the OUD has stabilized.

Recognize alternate-day dosing as an option for patients who are clinically stable at doses less than or equal to 12 mg per day (i.e., 24 mg every other day) and who require less frequent visits to the pharmacy for dosing.

- This practice should be balanced with the challenges in managing missed doses, and the patient should be assessed for toxicity/sedation when given this higher dose. Timely communication with the pharmacist is critical.
- If the main reason for considering alternate-day dosing is to facilitate fewer pharmacy visits, assess whether take-home doses or switching to an extended-release formulation are a superior approach with your patient.

Discuss the option of switching to buprenorphine extended-release monthly injection or the six-month subdermal buprenorphine implant to enhance medication adherence and convenience for patients who are clinically stable.

- Recognize that there is not yet evidence about the long-term safety and effectiveness of depot or implant buprenorphine therapy, and counsel the patient accordingly.
- Consider subcutaneous injection if the patient has been stabilized on 8–24 mg sublingual bup/nlx daily for at least seven days. The injection does not require abstinence from other opioids before initiation, but it is preferable.
- Consider the subdermal implant if the patient has been stabilized on 8 mg or less of sublingual bup/nlx daily. The implant requires a period of abstinence from opioids before initiation.

Discuss switching to buprenorphine injection or implant if the patient also:

- requires less frequent medication administration
- is comfortable with an invasive procedure or device
- does not want to administer medications sublingually
- has drug coverage if the medication is not covered by public health insurance.

Review current evidence for buprenorphine extended-release injection and the six-month buprenorphine implant before discussing them with patients so that you can provide adequate counsel in obtaining informed consent for these newer options.

Clinical recommendations for prescribers

UDT and take-home doses

Conduct UDT at least monthly during induction and dose escalation until the patient has reached a stable dose. UDT is useful to characterize risk and give the patient and the prescriber information about other hazard exposures, including interacting substances such as benzodiazepine receptor agonists (BZRAs) and other opioids. It is also useful in the context of take-home dosing.

Missed doses[1]

For missed doses with no relapse to full opioid agonist use:

- ≤ 5 days: resume previous dose
- ≥ 6 days: adjust the dose based on the total daily dose and number of missed doses; for example:

Missed days	Dose	Suggested adjustment
≥ 6 days	2 mg/0.5 mg–4 mg/1 mg	No change
≥ 6 days	6 mg/1.5 mg–8 mg/2 mg	Restart at 4 mg/1 mg
6–7 days	> 8 mg/2 mg	Restart at 8 mg/2 mg
> 7 days	> 8 mg/2 mg	Restart at 4 mg/1 mg

- 2 alternate-day doses: suspend bup/nlx until the patient can be reassessed. Then return the patient to a daily dose schedule, possibly at a lowered dose, to restabilize them before resuming an alternate-day schedule.

For missed doses due to relapse or return to full agonist opioid use: advise the patient to stop using bup/nlx until they are ready to resume OAT. Schedule a new induction date and proceed as described in the "Induction phase" section above.

B3. Prescribing methadone

Standards & frameworks for care

Methadone is prescribed in a way that balances the risk of adverse effects to the patient and people in their environment while optimizing the benefits, including retention in treatment and decreased health and quality-of-life harms related to substance use.

Clinical recommendations for prescribers

Induction phase (usually first two weeks)

Prescribe an initial dose of 10 mg or less; then increase doses by no more than 5 mg every five days (as necessary) for patients who:

- are recently abstinent or use intermittently
- have unknown tolerance to opioids due to unclear history or lack of collateral information
- use low-potency opioids (e.g., codeine).

[1] This section is adapted with permission from *A Guideline for the Clinical Management of Opioid Use Disorder* © 2017 British Columbia Centre for Substance Use.

Clinical recommendations for prescribers

Prescribe an initial dose of 5–20 mg; then increase doses by 5–10 mg every three to five days (as necessary) for patients who:

- have established tolerance via patient history or collateral information (e.g., UDT results)
- have risk factors that include:
  - high or multiple CNS depressant use (e.g., alcohol, antipsychotic, benzodiazepine, gabapentinoid)
  - medical illness involving respiratory compromise (e.g., chronic obstructive pulmonary disease)
- have changes in drug metabolism (e.g., over age 65, taking medications that inhibit CYP450 3A4).

Prescribe an initial dose of 5–30 mg; then increase doses by 5–15 mg every three to five days (as necessary) for patients who both:

- have high tolerance of high-potency opioids from daily use and have UDT confirmation of recent opioid use
- do not have risk factors for excessive CNS depression (as listed above).

Consider using a limited duration of SROM for outpatients and immediate-release oral morphine for inpatients to manage emergent withdrawal while titrating methadone dosing to reach a clinically therapeutic outcome (24 hours without any withdrawal or need for supplemental morphine).

Exercise extreme caution if you are considering rapid and high dose titration (increasing the methadone dose by more than 10 mg at a time in a period under five days).

- Consult with a colleague who has experience with rapid and high dose titration.
- Conduct a risk-benefit assessment for patients with high tolerance of high-potency opioids for whom slower titration could jeopardize retention in treatment.
- Monitor the patient closely, with direct assessment before each dose increase and assurance that the patient has a reliable and involved third party available for frequent contact and check-ins for early detection of methadone toxicity.

Reassess patients frequently during the first two weeks of treatment because they are at the highest risk of fatal overdose during this period. Discuss this risk and strategies to reduce it (e.g., use only small amounts of additional opioids; do not use alone; have a naloxone kit available). Document these discussions and reassess the patient with every subsequent dose increase.

Titration and stabilization phase

Increase the dose by 5–10 mg every five to seven days to manage withdrawal symptoms and cravings.

Clinical recommendations for prescribers

Maintenance phase

Use clinical judgment to determine an appropriate maintenance dose, with treatment objectives generally being to provide 24 hours without opioid withdrawal and to reduce opioid cravings while not causing sedation or toxicity.

Consider tapering down the dose for patients experiencing opioid-induced side effects (e.g., sweating, hypogonadism, severe constipation, adrenal insufficiency) and collaborate with the patient to balance the benefits, disadvantages and risks of methadone treatment.

If rapid metabolism is suspected, confirm with serum methadone levels (with peak/trough ratios > 2:1, wherever possible and available). If not possible, schedule an observation at a time when the emergence of withdrawal can be witnessed after an observed dose.

Adjust treatment accordingly (e.g., split dosing). Split dosing often requires providing evening doses as take-home doses because few patients will be able to attend a pharmacy twice daily for witnessed dosing. Consider clinical stability before offering split dosing, and consult with experienced colleagues on such challenging cases. There is no consensus on the best way to assess the need for split dosing.

Assess for post-dose sedation at peak serum levels for patients on high doses of methadone by arranging a witnessed dose in the pharmacy, with a follow-up in the clinic two to four hours later.

UDT and take-home doses

Conduct UDT monthly during induction and dose escalation until the patient has reached a stable dose. Conduct UDT more frequently to confirm abstinence from illicit opioid use and absence of interacting substances such as BZRAs, or in the context of take-home dosing. During stabilization, both scheduled and unscheduled UDT should be used, as appropriate.

Missed doses

- 1 or 2 doses: do not reduce the dose unless there are concerns about loss of tolerance or adverse events
- 3 doses: decrease the dose by 50 per cent
- 4+ doses: decrease the dose to 30 mg or less.

Re-establish a stable methadone dose in cases of several missed doses, as appropriate. This may not be the same as the previous dose.

Offer one replacement dose of methadone (no more than 50 per cent of the regular dose) if the patient has emesis that was witnessed by a health care provider and that occurred within 15 minutes of an observed dose.

- Where emesis can occur due to pregnancy, consider spreading the dosing over 30 minutes. In addition, if emesis is emerging as a recurrent reason for dose replacement, observation for 15 to 20 minutes after dosing may be warranted.

B4. Prescribing slow-release oral morphine[2]

Standards & frameworks for care	Slow-release oral morphine (SROM) is available for patients for whom bup/nlx and methadone have been ineffective or are contraindicated or refused.
Clinical recommendations for prescribers	Consider switching to SROM if the patient: ▪ is an adult with severe OUD ▪ has not responded to bup/nlx or methadone, has contraindications to their use or has refused bup/nlx and methadone. Consult with a specialist if you lack experience in prescribing SROM before initiating treatment. SROM treatment requires diligent measures to avoid overdose and diversion. Review risks and benefits with the patient, obtain fully informed written consent and ensure rigorous clinical documentation when prescribing SROM. Understand that evidence supporting the safety and efficacy of SROM in pregnancy is limited. However, this option can be considered at the discretion of the prescriber, weighing the risks and benefits and ensuring discussion of this use with the patient during the consent process. Prescribe SROM as once-daily witnessed doses (24-hour formulation) to prevent misuse and minimize diversion risk. Exceptions may be considered if the patient shows exceptional and sustained improvements in clinical and social stability. Review instructions for witnessed ingestion with the dispensing pharmacy because crushing, chewing or dissolving SROM pellets can cause a fatal overdose. Capsules should be opened by the pharmacist and the pellets given to the patient to swallow with water. **Induction and titration phase** Start with a one-week titration phase aimed at achieving a stable daily dosage. Separate dosage increases by 48 hours because of the slow-release properties of SROM.

[2] The sole existing guideline that was reviewed for this section was *A Guideline for the Clinical Management of Opioid Use Disorder*, developed by the British Columbia Centre on Substance Use and released in 2017. Many of the recommendations in this section were originally made in that guideline or have been adapted from it. The BCCSU is currently updating its SROM recommendations.

Clinical recommendations for prescribers

For patients using opioids other than methadone (e.g., heroin), prescribe 30–60 mg on the first day and titrate upward according to withdrawal symptoms. Note that in some patients and communities with high rates of illicit fentanyl use, higher doses such as 100–200 mg may be needed to retain the patient in care and mitigate withdrawal.

For patients who are switching from methadone to SROM, prescribe a methadone-to-SROM dose ratio of 1:4 on the first day (e.g., 60 mg methadone = 240 mg SROM) and titrate upward based on withdrawal symptoms and cravings. The ultimate stabilization dose ranges from 1:6 to 1:8.

Use clinical judgment to determine each dose increase. Consider the type of opioid the patient is using, their level of tolerance to opioids and the risk of overdose and diversion versus the risk of lower treatment retention. This clinical judgment is necessary given the current lack of published evidence for optimal SROM dosing.

- Some guidelines recommend titrating upward by 30–60 mg every 48 hours; however, the actual dose should be based on clinical response, type of ongoing opioid use and risk of leaving treatment.
- The average total daily SROM dose range is 200–800 mg per day. The full range reported in the literature is 60–1200 mg per day.

Stabilization phase

Stabilize the once-daily dose at the lowest dose needed to relieve withdrawal symptoms and suppress illicit opioid use. Currently, there is no literature to guide treatment decisions beyond the 36-week duration of clinical trials. In the absence of established guidelines, follow similar stabilization and tapering practices as are used for bup/nlx and methadone.

UDT and take-home doses

Note that point-of-care UDT may not rule out use of illicit heroin or some prescription drugs (e.g., morphine, codeine) in patients on SROM. Consult with testing laboratories about using mass spectrometry UDT.

Prescribe take-home doses only in exceptional circumstances, where patients show high clinical stability, or when daily witnessed dosing is a barrier to treatment. Consider graduated take-home dosing on a case-by-case basis, using clinical judgment, appropriate monitoring and follow-up to prevent misuse or diversion. Before prescribing, conduct a comprehensive risk assessment and consult a specialist.

Conduct UDT monthly, or more frequently when prescribing take-home dosing.

Clinical recommendations for prescribers

Missed doses[3]

Work closely with pharmacists to mitigate the risk of over-sedation or overdose caused by rapid loss of tolerance that can result from missed doses of SROM.

Use clinical judgment and consider total daily dose and number of missed doses in determining adjustments after missed doses. Various approaches are available; for example:

Missed days	Missed dosing schedule	
	Prescribed dose = 200 mg	Prescribed dose = 800 mg
1	200 mg	800 mg
2	120 mg (40% reduction)	480 mg (40% reduction)
3	80 mg (60% reduction)	320 mg (60% reduction)
4	40 mg or starting dose (e.g., 60 mg), whichever is higher (80% reduction)	160 mg (80% reduction)
5	Resume at initiation dose (e.g., 60 mg)	Resume at initiation dose (e.g., 60 mg)

See patients daily to assess for intoxication or withdrawal because there is a lack of clinical experience and clinical trials with SROM. Re-titrate accordingly.

B5. Prescribing injectable opioid agonist therapy[4]

Standards & frameworks for care

Supervised injectable OAT (iOAT), using diacetylmorphine or hydromorphone, is available for patients who continue to inject opioids despite adequate trials of methadone and buprenorphine.

Embedded wrap-around care is the preferred model for delivering iOAT. Treatment is integrated with services at community health centres, harm reduction programs and supportive housing programs to reduce barriers to treatment and address a range of health and social needs.

[3] This section is reprinted with permission from *A Guideline for the Clinical Management of Opioid Use Disorder* © 2017 British Columbia Centre on Substance Use.

[4] The sole existing guideline that was reviewed for this section is *National Clinical Guideline – Injectable Opioid Agonist Treatment: iOAT for Opioid Use Disorder*, developed by the Canadian Research Initiative in Substance Misuse and released in 2019. Many of the recommendations in this section were originally made in that guideline or have been adapted from it.

Clinical recommendations for prescribers

Consider switching to supervised iOAT for patients whose eligibility includes the following:

- confirmed and documented history of injection opioid use and severe OUD
- capacity to consent to treatment and to understand what it involves, including potential risks and side effects
- ability to attend for dosing regularly (up to three times daily) and ability to self-administer doses or to accept them from a provider or peer
- adequate trials of oral OAT without achieving a therapeutic dose, or ongoing health or social consequences related to OUD and continued injection opioid use
- high risk of medical consequences of injection opioid use.

Exercise caution in prescribing iOAT to:

- youth (under age 25) and older adults (over age 65)
- pregnant women or women who become pregnant while on iOAT
- patients with moderate or severe alcohol use disorder or benzodiazepine use disorder and those prescribed BZRAs
- patients with chronic medical conditions (e.g., respiratory, hepatic or renal disease, acute conditions, recent head injury, bleeding disorders).

Medication selection and administration

Provide iOAT as an open-ended treatment, balancing the benefits and risks, with decisions made in collaboration with the patient. If the patient is currently receiving oral OAT, consult with the oral OAT prescriber as part of the assessment process.

Choose between hydromorphone and diacetylmorphine based on availability, patient preference and clinical judgment. Consulting a pharmacist will alert you to prescribing or availability restrictions (security, disposal, preparation, inventory management, documentation requirements).

Supervise self-administered injection, which should involve a pre-injection assessment, direct observation of the injection and disposal of equipment, and a post-injection assessment.

Induction and titration phase

Start iOAT with three doses per day, in general. Adjust the initial dose over a two- to five-day titration period following this protocol:

- For hydromorphone, it is recommended that each dose be increased by 10 mg, to a maximum increase of 30 mg per day.
- For diacetylmorphine, it is recommended that each dose be increased by 20 mg, to a maximum increase of 60 mg per day.

Clinical recommendations for prescribers

Lower the dose or follow a more gradual titration based on the patient's response and safety concerns. Doses can be increased, as long as they are well tolerated, until they reach clinical effect (no use or reduced use of illicit opioids, no cravings) or the patient reaches the following recommended dose maximums:

- hydromorphone: 500 mg per day (maximum 200 mg per dose)
- diacetylmorphine: 1000 mg per day (maximum 400 mg per dose).

Recognize that these titration protocols and doses may not be enough to ease withdrawal symptoms and cravings in patients with very high opioid tolerance due to fentanyl. (See Appendix 7 in the CRISM iOAT clinical guideline for classic and alternative titration protocols.)

Stabilization and maintenance phase

Consider co-prescription of methadone or SROM to prevent withdrawal and cravings between iOAT doses (i.e., overnight).

Provide comprehensive and continuing care that involves ongoing review and assessment of dosage, side effects, drug interactions, patient goals, physical and mental health and psychosocial functioning.

Recognize that ongoing substance use while on iOAT may be an indication to intensify treatment, which may include increasing the dose of the sustained-release OAT, implementing a more intensive model of care or increasing psychosocial and other supports.

UDT and take-home doses

Recognize that regular and random UDT, which is considered standard care for oral OAT, is not standard care for iOAT because the risk of diversion is low and the patient has frequent contact with care providers. However, UDT can be used as a starting point for discussing harm reduction and safety.

Avoid take-home dosing for iOAT. Supervised administration ensures patient safety before and after treatment is administered and increases public safety by preventing diversion.

Missed doses

Be vigilant in supervising missed doses due to the short-acting nature of iOAT medications.

- If a new, not-yet stabilized patient misses three consecutive doses or one day (whichever is first), restart the titration process, following the titration protocol in Appendix 7 of the CRISM iOAT clinical guideline.
- If a stabilized patient misses six consecutive doses or two days (whichever is first), you may be able to provide their usual dose or a reduced dose. See Appendix 8 of the CRISM iOAT clinical guideline for an example of a dose reduction protocol.
- If a stabilized patient misses nine consecutive doses or three days (whichever is first), re-titrate entirely, following the titration protocol in Appendix 7 of the CRISM iOAT clinical guideline.

B6. Prescribing take-home doses

Standards & frameworks for care	Clinical risk assessment and management are used to support patient autonomy and social engagement while respecting patient and public safety.
Clinical recommendations for prescribers	Support flexibility in treatment with take-home doses unless you estimate that the benefits are exceeded by the risk of: ▪ toxicity from dosing errors ▪ harm to susceptible individuals in the patient's environment from exposure to the patient's agonist therapy ▪ therapy becoming ineffective due to medication non-adherence ▪ victimization of the patient by others in their environment. These risk estimations should take into account the possibility of: ▪ substance interactions (prescribed; non-prescribed; over-the-counter; illicit; licit, including alcohol) ▪ un/intentional diversion and possible exposure to susceptible individuals ▪ precarious social situations. Consider that given the inherent safety of bup/nlx over methadone, the schedule for take-home doses can be faster and based on clinical judgment. Consider prescribing take-home doses of methadone after two consecutive months of clinical stability (usually including reassuring UDT results). Implement a graduated take-home dosing schedule, rather than providing all doses at once. Prescribe one additional take-home dose every one to four weeks (if necessary), to a maximum of six methadone or 13 bup/nlx take-home doses at a time. ▪ Exceptions to these limits may be considered if a thorough assessment determines that they will promote treatment goals (e.g., productivity, involvement in recovery work) without risking patient and public safety. Prescribe such that the patient receives a witnessed administration of agonist therapy by pharmacy staff each time they pick up take-home doses. Transition from frequent to less frequent UDT (e.g., weekly to monthly) as the treatment dose is stabilized, a trusting relationship is established and goals relating to health and quality of life are consolidated. This practice facilitates the patient's engagement in important aspects of their life while providing information about treatment progress, medication adherence and safety. Facilitate guest dosing (i.e., arranging for the patient to temporarily receive their dose from a different pharmacy) in patients for whom take-home dosing may not support treatment safety and effectiveness, or who are unable to attend their regular pharmacy for an extended time. Collaborate with local pharmacies when necessary (e.g., if the patient is going out of town for a long period). Reduce or discontinue take-home doses if the patient experiences changes in clinical or social stability that increase the risk of adverse outcomes related to treatment safety and effectiveness.

Part C: Providing opioid agonist therapy in specific settings and populations

C1. Rural and remote settings

Standards & frameworks for care	All patients with OUD have access to OAT, meeting jurisdictional standards within 48 hours in their communities. Lack of psychosocial services is not a barrier to initiating and continuing OAT.
Clinical recommendations for prescribers	Collaborate with available services to prescribe OAT in a safe and accessible way for the patient, regardless of geographical location. Be prepared to initiate OAT using novel approaches such as telemedicine in partnership with local resources (e.g., nurse practitioners). Recognize bup/nlx as the best option for improving treatment retention and outcomes in areas where access to care is limited and daily witnessed ingestion of methadone at a pharmacy is not practical. Consider monthly injections of buprenorphine to reduce barriers to care and increase retention in treatment.

C2. Virtual care (telemedicine)

Standards & frameworks for care	All patients with OUD have timely access to OAT in their communities and do not face barriers related to health systems infrastructure (e.g., lack of access due to geography, physical disabilities).
Clinical recommendations for prescribers	Make arrangements when providing access to OAT using remote health care technology to ensure: ▪ continuity of agonist therapy without interruption due to pharmaceutical supply, pharmacy closures or public health emergencies ▪ ability of local health care providers to assess and manage emergencies (e.g., medication toxicity) ▪ availability of ancillary non-pharmacological addiction treatment and recovery services ▪ support of a local clinical resource (e.g., nurse practitioner, pharmacist) who can collaborate on providing OAT and ongoing assessment and assistance. Ensure that a focused physical assessment is completed early in treatment to identify conditions that can complicate substance use or that can affect OAT outcomes.

C3. Pregnant and postpartum women

Standards & frameworks for care	All pregnant or postpartum women with OUD are offered OAT on an urgent basis.
Clinical recommendations for prescribers	Understand your child-safety obligations and obligations to maintain confidentiality of patient health information, except in rare cases. Be familiar with local child–family services and develop working relationships with them if possible to encourage interventions that optimize supports for patients to keep their children, in most cases (for patients who choose to do so). Consider your familiarity and relationship with local child–family services in deciding whether to encourage patients to disclose their pregnancy. Some services may intervene in ways that are not beneficial to patients or their children, but programs do exist that prepare patients for parenting and help them to navigate prenatal care and benefits. Recommend against undergoing opioid withdrawal during pregnancy. Determine which type of OAT to use by considering the patient's circumstances, as well as treatment access and availability. Offer methadone or bup/nlx as first-line options for OAT during pregnancy. Recognize that unless it is clinically indicated or requested by the patient: ▪ transitioning between methadone and bup/nlx during pregnancy and postpartum is not recommended for patients who were stable on one of these medications before becoming pregnant ▪ transitioning pregnant patients from bup/nlx to buprenorphine monotherapy is not necessary. Manage opioid withdrawal symptoms by increasing the dose of bup/nlx or methadone and/or administering in divided doses until the postpartum period. ▪ Consider split doses of methadone and buprenorphine, especially in later pregnancy, due to enzyme induction, reduced elimination half-life and increased volume of distribution. Dose increases may be avoided by dividing doses (i.e., two, three or four times daily). ▪ Consider take-home doses of methadone for split dosing even in pregnant patients who may not otherwise be offered them if improved neonatal outcomes and reduced illicit substance during pregnancy justify the potential risks of take-home dosing. ▪ Ensure adequate analgesia (opioid and maximized non-opioid pharmacotherapies) during delivery, in addition to any OAT prescribed for baseline needs. ▪ Monitor patients closely postpartum for the need to reduce the methadone dose.

Clinical recommendations for prescribers	Encourage breastfeeding in general for women on OAT, unless there is a contraindication. Support women in considering all relevant medical and social factors when weighing the benefits and potential harms of breastfeeding. Patients who are breastfeeding and have a lapse to substance use on rare occasions should be advised to discard breast milk for 24 hours and then resume breastfeeding. Be familiar with the excretion of various substances in breast milk. The amount excreted is insufficient to treat neonatal withdrawal. Encourage rooming-in as the standard of care for opioid-exposed infants. Assess and treat neonatal opioid withdrawal symptoms in rooming-in settings, which provide an environment that promotes maternal–neonate attachment.

C4. Patients who are hospitalized

Standards & frameworks for care	Patients are never subjected to unnecessary withdrawal or forced detoxification. OAT is always maintained during hospital admission to prevent loss of tolerance and unnecessary withdrawal unless there is a contraindication. Hospital-based prescribers prioritize early identification and intervention in patients with high-risk substance use, including those who meet criteria for OUD. Patients are offered treatment and recovery options across the care continuum, including harm reduction resources and immediate initiation of OAT. Hospital-based prescribers recognize the need to treat withdrawal if OAT is not immediately available to or accepted by the patient. Symptomatic treatment, which may include bup/nlx, non-opioids and short-acting opioids such as morphine sulphate, is offered to ease withdrawal while assessments and long-term treatment are being determined. Patients receive care in a non-judgmental environment that supports safety and treatment adherence, and that recognizes that some patients may continue to use substances while hospitalized.
Clinical recommendations for prescribers *Note: These recommendations are for prescribers working in a hospital setting.*	Order an ECG if clinically indicated (e.g., the patient is on more than 120 mg of methadone or has risk factors for prolonged QTc). Communicate with the patient's community pharmacy to: ▪ verify the patient's current dose and the date it was last observed ▪ determine whether the patient is receiving take-home doses and when they were last dispensed ▪ discuss the pharmacist's assessment of the patient's stability ▪ cancel any outstanding prescriptions for OAT to minimize risk of double dosing during hospitalization or upon discharge.

Clinical recommendations for prescribers	Notify the patient's regular OAT prescriber on admission and collaborate to: ▪ cancel any outstanding prescriptions for OAT ▪ ensure that changes in therapy are documented to reduce risk ▪ discuss dosage increases and decreases before implementing them, when possible (consult another OAT prescriber if communicating with the regular prescriber is not possible). Monitor for the emergence of confounding factors during the patient's hospital stay (e.g., drug interactions, drug–disease interactions) and adjust the OAT dose accordingly. Consider split dosing if there is neurological, respiratory or hepatic compromise. Collaborate with the patient, prescribers, pharmacy team and support network to ensure access to a range of care options that build on the treatment experience and that address key social determinants of health that support ongoing engagement in OAT. Facilitate seamless and safe transfer of care to the regular prescriber and community pharmacy upon discharge. In some jurisdictions, hospital-based clinicians who do not have OAT prescribing approvals cannot write the discharge prescription, so early coordination with community prescribers or an addiction consultation team is important, especially if discharge is premature or unexpected. Initiate OAT in hospital whenever possible for patients who are diagnosed with OUD after admission. Collaboration with the care team that will continue the patient's OAT in the community is critical to a successful transfer of care.

C5. Patients who are incarcerated

Standards & frameworks for care	Patients are never subjected to forced detoxification. OAT is always maintained during incarceration to prevent loss of tolerance and unnecessary withdrawal. Care standards in correctional settings meet those of treatment standards in the community. The trusting therapeutic relationship between OAT prescriber and patient remains the focus of treatment, despite challenges associated with providing care in a correctional setting. Community resources (e.g., OAT programs, experienced colleagues) are readily available for prescribers who work in correctional facilities. Harm reduction resources and services are provided in correctional settings for patients who use substances, and OAT is offered to patients with OUD who are using those resources if they meet criteria for this treatment.

Clinical recommendations for prescribers	The patient's regular OAT prescriber should do the following, when requested by the correctional facility: ▪ Provide all information necessary for safe and effective OAT. ▪ Collaborate with the prescriber working in the correctional facility and with the community pharmacist, if applicable, to ensure continuity of care before (and at the time of) release. The prescriber working in a correctional facility should do the following: ▪ Contact the patient's community pharmacy to determine the patient's current dose and date of last dose. ▪ Make every effort to provide continuity of care with the patient's regular OAT prescriber. ▪ Make every attempt to educate the patient about the potential for relapse and the dangers of overdose, particularly in the lead-up to release. The patient should receive a take-home naloxone kit and overdose prevention training prior to release. ▪ Encourage adherence to treatment by supporting the patient's regular dosing schedule and monitoring for potential missed doses (e.g., during events such as court appearances). ▪ Maintain an up-to-date medical chart for the patient (including UDT results). ▪ Avoid discontinuing OAT simply as a consequence of non-reassuring UDT results. ▪ Collaborate with the patient's regular OAT prescriber and pharmacy team before release to provide an update on: ‣ discharge plans that have been made with the patient and support networks (e.g., harm reduction strategies, provision of a naloxone kit, referrals to community organizations that address social determinants of health) ‣ any changes in dosage ‣ prescribing of short-term opioid analgesics, psychoactive drugs or medications with the potential to interact with OAT. ▪ Assist the patient in arranging to continue OAT upon release: ‣ Communicate with the patient's regular OAT prescriber and give the patient a valid prescription to take to their pharmacy until they are able to see their regular prescriber. ‣ Ensure that a patient who was not on OAT or did not have a regular OAT prescriber prior to incarceration is connected with a prescriber and a pharmacy before release.

C6. Transition-aged youth

Standards & frameworks for care	Considerations are made to ensure that patients navigating between adolescent and adult health care services receive adequate and age-appropriate OUD treatment.
Clinical recommendations for prescribers	Consult an experienced colleague to assist with assessing the role of OAT if you do not have the knowledge, skills or resources to treat adolescents with OUD. Whenever possible, prescribers should have experience working with this population and should collaborate with youth counsellors. Encourage and facilitate engagement in non-pharmacological treatment (e.g., recovery-oriented services) to complement OAT. You should be familiar with the programs to which you refer adolescents and feel comfortable that they offer evidence-based treatments that support patients on OAT. Consider bup/nlx as first-line treatment for moderate-to-severe OUD in youth.

Part D: Providing opioid agonist therapy for patients with co-occurring disorders

D1. General considerations

Standards & frameworks for care	Prescribers recognize that patients with OUD often have other ongoing health concerns, and support is provided to appropriately manage those concerns.
Clinical recommendations for prescribers	Encourage patients to attend a primary care provider or team for ongoing preventative care and chronic disease management. Communicate openly and regularly with the patient's primary care provider.

D2. Mental health and addiction considerations

Standards & frameworks for care	Patients with OUD who also have a mental health disorder or another substance use disorder are offered concurrent treatment.
Clinical recommendations for prescribers	Screen and assess OAT patients for mental health disorders (e.g., anxiety, depression, posttraumatic stress disorder [PTSD], personality disorders) and suicidal ideation. If they do not respond to primary care–led treatment or if they require specialized care, refer them to a mental health professional, and reassess them during the course of OUD treatment. Screen patients for trauma and abuse (past or current) and refer them to counselling if they express interest. Assess patients periodically for alcohol, nicotine and other substance use, and offer appropriate psychoeducation and treatment. Using cannabis, stimulants or other addictive substances should not be a reason to suspend OAT. Avoid co-prescribing BZRAs to patients on OAT due to increased risk of respiratory depression, daytime hypersomnolence, cognitive disturbance and overdose death. If clinical assessment, preferably by an addiction psychiatrist, suggests that a trial of BZRAs may be warranted, be aware of the interaction between the BZRA and OAT, adjust the dose and timing accordingly, and dispense only small amounts at a time.

Clinical recommendations for prescribers	Evaluate the indication for OAT patients who are already on long-term BZRAs. The decision to continue prescribing or to de-prescribe the BZRA needs to be made with attention to other confounding diagnoses, including sedative use disorder and PTSD. ▪ If prescribed for insomnia, BZRAs are indicated only for short-term intermittent use; therefore, a slow and gradual taper can be considered. ▪ If prescribed for anxiety, BZRAs need to be used in a way that reflects guidelines for treating anxiety disorders. Prescribing and monitoring should be done together with clinicians who are familiar with BZRA–OAT interactions, overdose risk and BZRA use disorder. ▪ If prescribed for PTSD, evaluate the risks and benefits because benzodiazepines can cause PTSD in patients who have recently experienced trauma and can perpetuate PTSD symptoms in those who have the disorder. ▪ Attempt to decrease the BZRA dose or taper the patient off the medication, particularly if they have respiratory disease or sleep-disordered breathing, show signs of misuse, are older adults or are on: ‣ multiple daily doses ‣ a high OAT dose ‣ other medications or substances with sedating properties. Collaborate with pharmacists to prevent, monitor and manage drug interactions between OAT and other prescription or non-prescription medications that a patient may be taking. Methadone interactions require particular attention. Be knowledgeable about local mental health and addiction resources, including wait lists, costs and practitioner expertise and approach in order to provide informed referrals that reflect patient needs and preferences.

D3. Infectious disease considerations

Standards & frameworks for care	Patient care includes preventative, screening and treatment measures (as needed) for sexually transmitted infections and infectious diseases, such as influenza, hepatitis and HIV, and other public health recommendations.
Clinical recommendations for prescribers	Screen for the following conditions when beginning OAT, once a year after that and more frequently if the patient has ongoing risk factors: ▪ hepatitis A and B, and arrange immunization ▪ hepatitis C and HIV, and offer referral and treatment as necessary (ongoing substance use is no longer a contraindication for hepatitis C treatment) ▪ sexually transmitted infections as indicated, and treat according to prevailing antimicrobial sensitivities.

Clinical recommendations for prescribers	Offer HIV pre- and post-exposure prophylaxis to patients who meet criteria to receive this preventative measure. Prioritize patients who face substantial risks of ongoing illicit substance use. When considering priority access to OAT, evaluate risks to the person, society and public health. Give priority access to untreated HIV-positive patients whenever possible due to the personal and public health consequences of untreated HIV infection. Dispense antiretroviral and hepatitis C treatment with OAT to improve medication adherence. Collaborate with pharmacists to prevent, monitor and manage drug interactions between OAT and other prescription or non-prescription medications the patient may be taking. Antimicrobial medications can significantly interact with OAT. Consult with a knowledgeable physician or pharmacist when providing OAT to patients with HIV/AIDS because some medications that treat HIV/AIDS can affect serum methadone levels. Counsel patients on ways to prevent reinfection.

D4. Acute and chronic pain considerations

Standards & frameworks for care	Prescribers are responsible for managing acute and chronic pain in their OAT patients whenever possible. Patients are supported in finding alternative pain treatments (including non-opioid pharmacotherapy and non-pharmacological therapy) that are financially and geographically accessible and culturally appropriate.
Clinical recommendations for prescribers	Explore non-pharmacological therapies for treating pain in OAT patients. Ensure that these therapies align with the patient's goals and values, and that they are culturally appropriate and financially and geographically accessible. Consider non-opioid analgesic options before opioid options. Avoid gabapentinoids for the treatment of chronic pain because there is limited evidence for their use in this context (other than for a few specific conditions) and there is a higher risk of mixed CNS depressant overdose in combination with opioid agonists. Avoid the patient's previously reported opioid of choice if prescribing opioids for acute pain. Dispense the opioid in small amounts (i.e., controlled dispensing, preferably daily) and limit the prescription to the number of days that opioids are typically needed for the specific acute pain condition.

Clinical recommendations for prescribers	Consider opioids in addition to bup/nlx or methadone for patients with acute pain that warrants short-term opioid therapy, and/or temporarily split the OAT dose and consider a temporary dose increase to cover the pain. Consider prescribing methadone in split doses for patients with severe chronic pain who require opioids. Usually this would only be done after the patient reaches a stable, once-daily dose and becomes eligible for take-home doses. If the patient is clinically stable, consider providing the second dose as a take-home dose. Consider formally or informally consulting with a pain specialist to enhance the patient's treatment plan if chronic pain persists after stabilization and optimization of OAT doses.

Part E: Discontinuing opioid agonist therapy

E1. Transferring care

Standards & frameworks for care	Maintaining patient safety is the primary concern when transferring care.
Clinical recommendations for prescribers	Share treatment progress notes with other providers involved in the patient's care if you have the patient's consent. Discuss plans for transferring care with the patient and the care team, including the pharmacy, and ensure that everyone involved has a clear understanding of roles, responsibilities and expectations. Support the patient in finding alternative OAT services if you are closing your practice, and begin well in advance to allow the patient to adjust. Make all reasonable efforts to help find a new prescriber if the patient is moving to another community. Supply clinical information to permit safe and effective continuation of OAT when fully transferring the patient's care to another prescriber. This information should include: ▪ reason for transfer ▪ OAT dosage ▪ prescribed medications ▪ patient's regular community pharmacy ▪ take-home dose flexibility ▪ UDT results ▪ treatment plan and goals ▪ ECG history (for patients on methadone) ▪ clinical history. Ensure that the new prescriber has access to the patient's information at the time of the transfer and at any time after that.

E2. Tapering and withdrawal management

Standards & frameworks for care	The choice to decrease the dose or discontinue OAT is made by the patient and provider after the patient has been fully informed of the possible consequences. Withdrawal management (i.e., detoxification without immediate transition to long-term addiction treatment) by itself is not recommended.
Clinical recommendations for prescribers	Recognize that the longer a patient is retained on OAT, the better the outcomes and the lower the risk of mortality. At least one year of stability on OAT is recommended before initiating a taper. Discuss the possible risks of discontinuing OAT because research shows high relapse rates and risk of fatal opioid overdose, even after long-term stability. Consider a slow taper approach (i.e., spread over months or years) for patients with a successful and sustained response to OAT who wish to discontinue OAT. Increase the frequency of patient contact to ensure adequate support during and after tapering. Offer relief of symptoms for patients who are in moderate or severe withdrawal from opioids by slowing the taper or increasing the dose of bup/nlx or methadone, or by prescribing non-opioid options (e.g., clonidine, loperamide, diphenhydrinate). Suggest attempting periodic tapers for patients on high OAT doses (e.g., more than 24 mg of bup/nlx or 120 mg of methadone) if there is low risk of relapse and the patient has been stable for at least one year. Avoid withdrawal management as a stand-alone treatment because it is associated with loss of tolerance and high risk of overdose death on discharge. This includes rapid inpatient tapers with methadone or bup/nlx. Patients in acute withdrawal should be offered pharmacotherapy to manage symptoms within two hours of presentation (see above for non-opioid options). Document discussions to ensure that the patient has made an informed decision about the risks and benefits of discontinuing OAT. Ensure that the patient leaves with a naloxone kit, and follow up for psychosocial support. Maintain an “open door” approach to care so that the patient feels welcomed back in case of relapse or if further support is required.

Key opioid use disorder treatment guidelines

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Health Quality Ontario. (2018). *Quality Standards. Opioid Use Disorder Care for People 16 Years of Age and Older*. https://hqontario.ca/portals/0/documents/evidence/quality-standards/qs-opioid-use-disorder-clinician-guide-en.pdf

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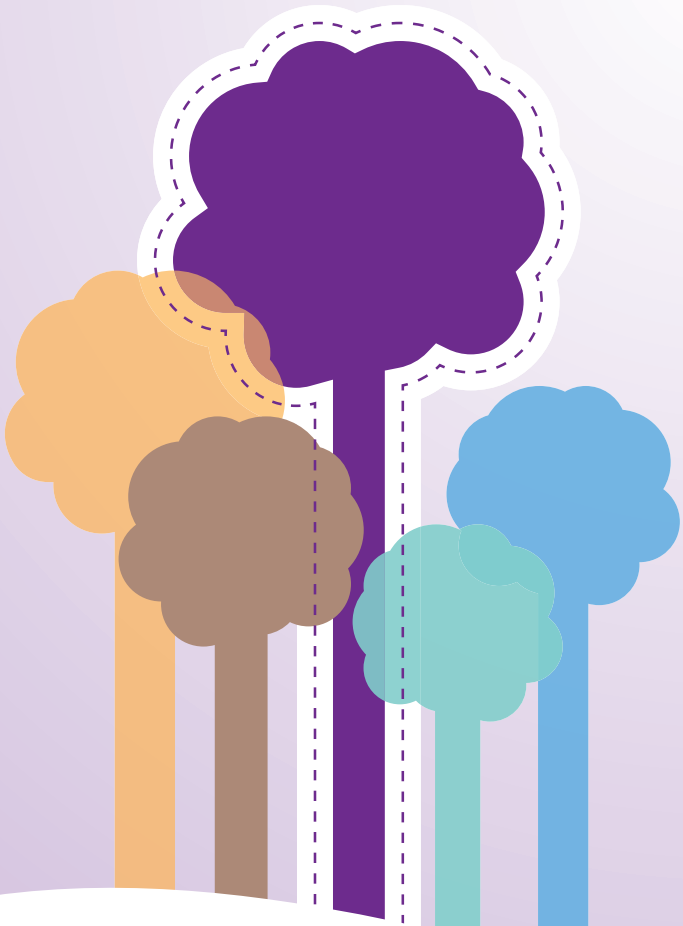

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