

Therapeutics Initiative

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Buprenorphine maintenance treatment for opioid use disorder

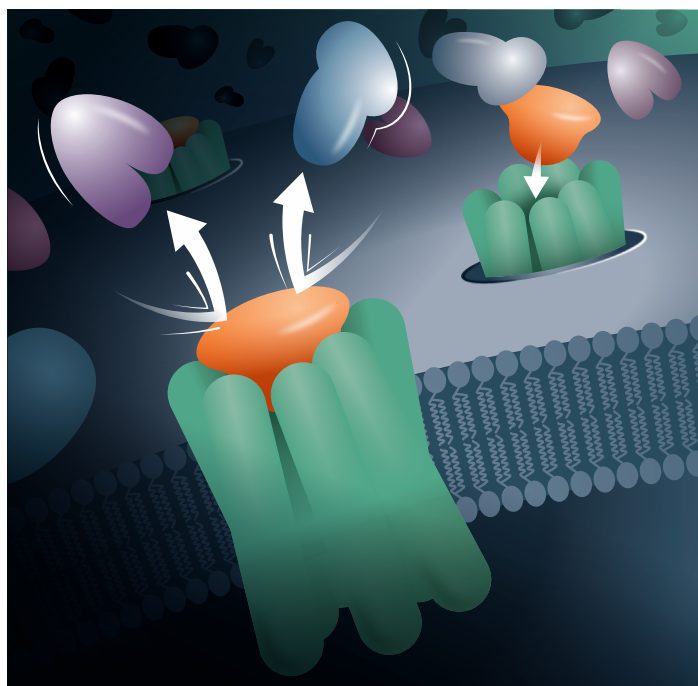
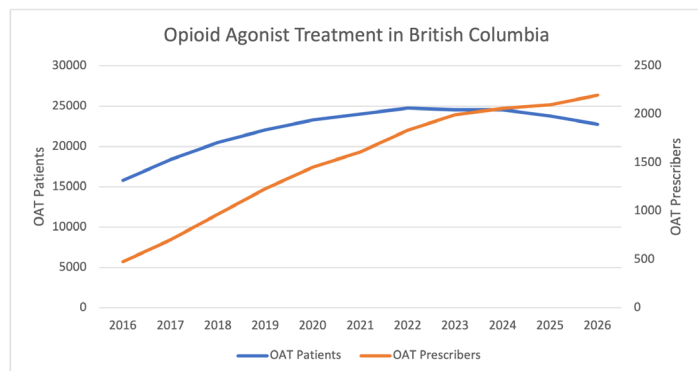
Vignette: Will is a 35-year-old male with a severe opioid use disorder (OUD). He reports smoking ¼ g of fentanyl per day for more than four years, and has experienced two non-fatal overdoses that required intervention with take-home naloxone. He recently sought help from the provincial opioid treatment access phone line, which started and titrated him to a dose of 24 mg of buprenorphine-naloxone SL once daily. His symptoms are well controlled on this dose and he is seeing you as his primary care provider for maintenance therapy. **What will you do?**

Key messages

- Opioid use disorder (OUD) has a prevalence between 1-2% of the adult population in BC, similar to the prevalence of other chronic conditions commonly managed in primary care settings.
- Opioid agonist treatment (OAT) such as buprenorphine-naloxone is the gold standard therapy that reduces mortality and improves quality of life.
- Without additional training or qualifications, family physicians and nurse practitioners can safely and routinely facilitate maintenance buprenorphine-naloxone therapy.
- Additional training available in British Columbia enables family physicians and nurse practitioners to prescribe additional OAT agents such as methadone and slow-release oral morphine.

Background and epidemiology

Approximately 100,000-125,000 British Columbians currently meet criteria for opioid use disorder (OUD).¹ Opioid agonist treatment (OAT) is the gold standard treatment for reducing morbidity and mortality.²



In British Columbia (BC), OAT prescribing rose from 15,774 patients per month in 2016 to over 22,000 per month in 2026, without a significant change in the overall prevalence of OUD. This shift was accompanied by an increase in OAT prescribers (Figure).³ However, a significant majority of eligible OUD patients are still not engaged in OAT. While this gap may be due in part to personal preferences and motivations, numerous health system factors also contribute to under-prescribing, including strict OUD program requirements, stigma, and lack of access to prescribers (particularly in rural and remote areas).⁴ Also of concern, OAT retention remains low, with fewer than 50% retained for 3 months and fewer than 20% lasting one year.⁵ This *Letter* was motivated, in part, by a recent Cochrane systematic review of 7 trials that showed OAT in primary care had good retention and opioid abstinence rates compared to specialist clinics.⁶ We do not review that evidence here, but provide practical, evidence-informed guidance to improve access to and continuation of OAT in primary care in BC.

Indicator	Trends	Getting better?
Fatal overdose	Declined since their peak in 2023, but still 3-4 deaths/day ³	✓
Non-fatal overdose	At an all-time high ³	✗
Opioid use disorder	Approximately 115,000 British Columbians are estimated to meet criteria ⁷	?
OAT access	Patients receiving OAT: 15,774 / month (2016) >22,000 per month (2026) ³	✓
OAT prescribers	Number of OAT prescribers has increased ³	✓
OAT uptake	Remains low, with only 1 in 5 individuals with OUD receiving OAT ⁸	✗
OAT retention	<50% retained at 3 months; <20% retained at one year ⁵	✗



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Canadian OUD guidelines strongly recommend either buprenorphine or methadone as first-line OAT.^{9,10} In BC, methadone prescribing for OAT (but not for pain) requires specific training and certification, but prescribing buprenorphine does not.⁹ All OAT medications are free to BC residents as regular Pharmacare benefits. Prescribing of OAT in primary care clinics results in equivalent morbidity and mortality outcomes compared to OUD clinics, with primary care settings also improving the management of co-morbidities and potentially increasing patient satisfaction and retention.^{6,11} A recent Cochrane review also found that abstinence from non-prescribed opioids at 3, 6, 12 or 24 months was higher with OAT in primary care than specialist clinics (RR 1.59, 95% CI 1.03 to 2.46).⁶

Buprenorphine is a “partial” long-acting mu-opioid receptor agonist. It is unique, relative to other opioids, in that it has a “ceiling effect”, resulting in much less respiratory depression and decreased risk of overdose.¹² As a partial agonist, it provides a weaker signal at the mu-opioid receptor, while at the same time its very high binding affinity blocks other opioids from stimulating these same receptors. The end result is that, when administered alone, it binds the mu-opioid receptor and provides a positive signal (agonist effect). Conversely, if given in the presence of other opioids such as morphine or fentanyl (either prescribed or non-prescribed), its high affinity outcompetes them, resulting in the attenuation or “blocking” of their mu-opioid activity (antagonist effect).¹²

Buprenorphine is administered sublingually, bypassing first-pass metabolism. It is metabolized in the liver into the active metabolite norbuprenorphine, and is primarily excreted in the feces.¹² In BC, as in most jurisdictions, sublingual buprenorphine is co-formulated with naloxone to disincentivize insufflation or injection use (naloxone is not orally bioavailable, thus has no significant effect if taken orally or sublingually) and comes in 2/0.5 mg and 8/2 mg tablets. Buccal films are also available in the same formulation and dosages, however they are not regular Pharmacare benefits. Once monthly extended-release subcutaneous injections are an alternate formulation that is indicated for maintenance OAT if preferred by patients. Buprenorphine is additionally available as a transdermal patch, though this formulation is used primarily for chronic pain management and is not dosed adequately for OAT.

Numerous strategies help to navigate the buprenorphine initiation process without triggering the antagonist effect and inadvertently putting a patient into opioid withdrawal (known as “precipitated withdrawal”). These include the use of wash-out periods for other opioids, or the gradual introduction of small, serially increasing doses of buprenorphine over a number of days (known as a “low dose induction”).⁹ Both the initiation phase, not detailed herein, as well as maintenance OAT, the focus of this *Letter*, can safely be managed by family physicians and nurse practitioners, and expert support is readily available (see below).

An appropriate maintenance dose should consistently curb withdrawal symptoms and cravings over a full 24-hour period. Maintenance doses typically range between 8 and 24 mg sublingually once daily, although up to 32 mg daily may be beneficial in some individuals.¹³

Once resolution of OUD symptoms is achieved, dose adjustments are not typically needed. If persistent or recurring cravings are experienced, doses can be increased rapidly without risk of overdose (e.g. 2-4 mg daily or more). Generally, outside of serious adverse effects, dose reductions should be slow (e.g. 1-2 mg weekly), accompanied by close monitoring for breakthrough cravings, or withdrawal symptoms.⁹

Due to the long half-life of buprenorphine (>24 hours), individual missed doses do not typically result in significant withdrawal symptoms. Following a single missed dose, continue at the same daily dose (i.e., do not give a “make-up” double dose). The reasons for missing the dose should be explored and addressed.

If more than 2-3 daily doses are missed, a patient may begin to experience breakthrough cravings, withdrawal symptoms, and/or a return to unregulated opioid use. If the patient returns to un-regulated opioid use they may need to formally re-initiate the medication, to minimize the risk of precipitating acute withdrawal.⁹ The *BC Opioid Use Disorder Guidelines* contain a helpful table providing direction on how to navigate these various missed dose scenarios.

<i>Missed days without return to full opioid agonist use</i>	
≤5 days	Resume without dose reduction
≥6 days	Re-titration is recommended to be individually tailored to achieve previous stable dose within a few days
<i>Missed days with return to full opioid agonist use</i>	
≤3 days	Safe to continue buprenorphine-naloxone without re-titration
4 days	Discuss the risk of precipitated withdrawal and weigh them against the benefits of continuing buprenorphine-naloxone
≥5 days	New induction may be required

Buprenorphine has considerably fewer side effects than other opioids, nonetheless common opioid-related adverse effects do occur. Drowsiness and sedation are rare and can usually be addressed with cautious dose reductions. Constipation is more common and can be managed with osmotic laxatives.¹⁴ Long term buprenorphine therapy has been associated with an increased risk of dental caries.¹⁵ Other adverse effects linked to long-term opioid treatment have not been studied rigorously

with buprenorphine, however providers should be aware of the potential for conditions such as obstructive sleep apnea and hypoandrogenism. There are no specific guidelines on how to manage these issues in the OUD population.

As buprenorphine is metabolized by the cytochrome pathway, other prescriptions or over-the-counter supplements that inhibit or induce the action of these enzymes (specifically CYP3A4) may alter buprenorphine levels and necessitate dose adjustments.¹² As with all opioids, unpredictable and/or synergistic effects require particular caution with other sedating and hypnotic medications. Other opioids will have muted effects due to buprenorphine's competitive antagonism, and are generally not recommended. Finally, buprenorphine can prolong QT intervals, but less than methadone.¹² This may require ECG assessment when combined with other QT-prolonging medications.

4. What other psychosocial resources are available?

OUD management is complex and includes dealing with medical and mental health co-morbidities, chronic pain, and psychosocial problems. Psychosocial supports range widely, dictated by local resources, context, and patient acceptance. These may include counseling, psychotherapy, peer-led support groups, and/or residential (or "bed-based") treatment.⁹

5. What if questions are asked about medication rotations, other treatment options, and/or tapering off OAT?

If patients find buprenorphine intolerable or ineffective, other OAT options are available including methadone and slow-release oral morphine. Family physicians and nurse practitioners can easily become familiar with these alternate treatment options and/or how to facilitate access to experts that provide safe transitions between these medications.

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Patients should generally be encouraged to stay on OAT long-term, if not indefinitely. Patients interested in stopping OAT should be counselled about the potential consequences, particularly the high proportion of relapses to unregulated opioid use and increased overdose risk.¹⁶ Dose adjustment and/or strategies to mitigate adverse effects should be actively pursued to prolong therapy.

In cases where patients are stable for greater than 1 year, are requesting a taper off of their medication, and are informed and accepting the potential risks, an individualized tapering plan can be considered. It is recommended, however, that this is led by an experienced OAT practitioner. If tapering is attempted, it should be small and gradual dose reductions over many months, accompanied by close supervision.^{9,16}

Clinical support and education resources

For further support, practitioners are directed to the **RACE** and the **24/7 Addiction Medicine Support Line** for direct access to consultative expertise. Additional online educational materials such as the **Provincial Opioid Addiction Treatment Support Program** are available online from the **BC Centre on Substance Use** and **UBC Continuing Professional Development**.

Links:

- <https://www.bccsu.ca/24-7/>
- <https://www.raceconnect.ca/>
- <https://www.bccsu.ca/provincial-opioid-addiction-treatment-support-program-poatsp/>