May 2016

Moving Towards Improved Access for **Evidence-Based Opioid Addiction Care**

in British Columbia

Recommendations from the British Columbia Node of the Canadian Research Initiative on Substance Misuse



BRITISH COLUMBIA CENTRE for EXCELLENCE in HIV/AIDS



Executive Summary

The declaration of a public health emergency in response to the recent rise in illicit drug overdose deaths in British Columbia underscores the importance of developing a coordinated, evidence-based provincial strategy to address the harms related to pharmaceutical and illicit opioids. A key component of this strategy is the delivery of health system interventions that optimize engagement, care and treatment of individuals with opioid addiction. This report briefly describes the scope of the provincial opioid crisis; how regulatory systems for opioid addiction treatment have evolved in BC, Canada, and internationally; and makes several recommendations that support the elimination of current barriers to accessing buprenorphine/naloxone, a safe and effective alternative to methadone for treatment of opioid addiction that is currently underutilized in BC.

Moving towards improved access for evidencebased opioid addiction care in British Columbia

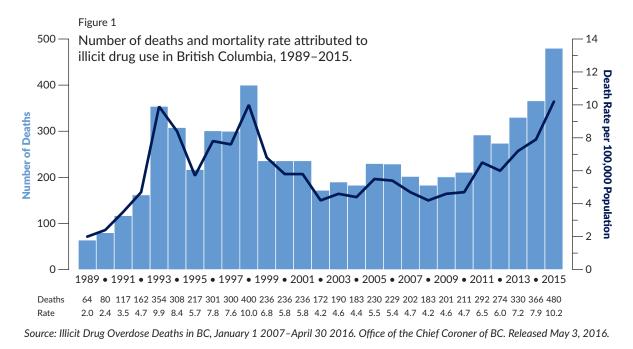
The declaration of a public health emergency in response to the recent rise in overdose deaths in British Columbia underscores the importance of developing a coordinated, evidence-based provincial strategy to address the harms related to pharmaceutical and illicit opioids. One key component of this strategy is the delivery of health system interventions that optimize engagement, care and treatment of individuals with opioid use disorder. Recent changes to BC PharmaCare that expand coverage to include buprenorphine/ naloxone (e.g., Suboxone[®]) as a first-line treatment for opioid use disorder (e.g., patients are no longer required to try methadone first) offer a promising step forward in reducing fatal overdoses, addiction and other severe harms related to opioid use in BC.¹ In addition, in coming months it is anticipated that the College of Physicians and Surgeons of British Columbia (CPSBC) may eliminate prescriber restrictions on buprenorphine/naloxone, which will further improve access to evidence-based care for all British Columbians. These changes present an opportunity to highlight remaining barriers to buprenorphine/naloxone access that persist despite clear research evidence of its safety and effectiveness.

This document briefly describes: the scope of the provincial opioid crisis; how regulatory systems for opioid addiction treatment have evolved in BC, Canada, and internationally; and the evidence base supporting elimination of barriers to accessing buprenorphine/naloxone in BC. Specifically, the best available evidence strongly supports a potential move by the CPSBC to remove the requirement that BC physicians must hold an exemption under section 56 of the Controlled Drugs and Substances Act (e.g., a "methadone exemption") in order to prescribe buprenorphine/naloxone. In addition, the evidence supports primary care and communitybased physicians having a more prominent role in prescribing buprenorphine/naloxone for the treatment of opioid use disorder, and adoption

of the dosing recommendations from the drug's product monograph in provincial opioid agonist treatment program regulations and guidance.²

Scope of the Problem. Surveillance data from the BC Coroners Service spanning 2006-2015 show a substantial increase in overdose deaths attributable to illicit drugs, including non-prescribed prescription opioid medications and heroin (Figure 1).3 In 2015, 480 illicit drug overdoses were reported across BC, representing a 31% increase from 2014.4 This translates to a mortality rate of 10.2 deaths per 100,000 population.⁴ Similarly high rates have not been observed since the 1990s during the height of the intravenous heroin epidemic in Vancouver.4,5 Although all provincial health regions showed an increase in overdose deaths, those outside of metro Vancouver were hit hardest, with the Interior and Fraser Health Authorities reporting a 30% and 50% increase in fatalities in the past year, respectively.3 These trends have continued into early 2016. In the month of January alone, 76 overdose deaths were reported in the province-the largest number of deaths in a single month in almost a decade.⁴

In response to the significant rise in illicit drug-related overdoses, and projections that approximately 700-800 overdose deaths are expected this year if trends continue unabated, provincial health officer Dr. Perry Kendall has declared a public health emergency.6 This is the first time a provincial health officer has served notice under the Public Health Act to exercise emergency powers, reflecting the severity of the current situation and the urgent need for collective action. BC is the only province in Canada to take this action to address the illicit drug overdose crisis, which will allow medical health officers throughout the province to collect robust, real-time information on overdoses to immediately identify localized patterns of risk, permitting immediate intervention to prevent serious harms and deaths among people who use drugs.



The recent emergence of fentanyl in the illicit drug market has contributed to the rise in overdose deaths, and is a pressing public health concern. Specifically, this highly potent synthetic opioid has been increasingly used to replace and/or "cut" heroin, oxycodone, and other illicit opioids. Fentanyl can be 50-100 times more toxic than morphine and is often ingested unknowingly, posing substantially higher risks of overdose-related harms and death than heroin or other illicit opioids? Preliminary data suggest that the proportion of illicit drug overdose deaths involving fentanyl (alone or in combination with other drugs) has rapidly increased from 5% in 2012 to approximately 30% in 2015.3 Of the 200 overdose deaths that occurred from January 1 to March 31 of this year, fentanyl has been detected in 98 cases (49%).8

While not all people who use opioids meet the criteria for opioid use disorder (i.e., addiction), it is critically important to expand access to addiction care and treatment for high-risk opioid users, in order to reduce overdose deaths in the province, and to target emerging threats to public safety such as the fentanyl trade.⁹

Regulation of Treatment Options for Opioid Use Disorder. There are currently two first-line pharmaceutical options available in BC for the treatment of opioid use disorder: methadone and buprenorphine/naloxone (e.g., Suboxone®). Methadone is a long-acting synthetic opioid that acts as a mu (μ) opioid receptor agonist. In BC, it is administered as an oral solution (e.g., Methadose®). When administered at a therapeutic dosage, methadone prevents opioid withdrawal, reduces opioid craving, blocks the euphoric effects of other opioids, and reduces mortality. Methadone has been available in Canada for treating opioid use disorder since the 1960s, although regulations were initially very restrictive.¹⁰ Federal regulations for methadone were relaxed in the 1990s, expanding access to treatment in an effort to reduce drug-related harms and HIV-transmission associated with injection opioid use, which had reached epidemic levels in Vancouver's Downtown Eastside.¹¹ Currently, methadone is classified as a controlled drug in accordance with section 56 of the Controlled Drugs and Substances Act, requiring physicians to be authorized to prescribe the medication via an exemption from the Federal Department of Health

Canada. BC has benefited from a well-established methadone maintenance program for the treatment of opioid use disorder, which is stewarded by an appointed panel of the CPSBC.¹²

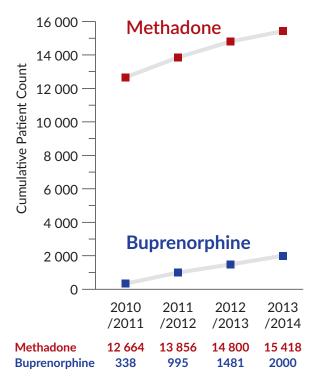
In recent years, buprenorphine/naloxone has emerged as viable alternative to methadone for treating opioid use disorder. Health Canada first approved buprenorphine/naloxone for the treatment of opioid dependence in adults in 2007. Buprenorphine/naloxone is a combined formulation of buprenorphine, a partial mu-receptor agonist, and naloxone, an opioid antagonist, which is administered as a sublingual tablet. Buprenorphine acts to prevent opioid withdrawal and craving, while the inclusion of naloxone is intended to deter non-medical injection and diversion. When buprenorphine/naloxone is taken as directed in sublingual form, its naloxone component has negligible bioavailability and the therapeutic effect of buprenorphine predominates.13 However, if diverted for injection use via subcutaneous, intramuscular, or intravenous routes, sufficient naloxone is absorbed to induce some withdrawal symptoms in active opioid users.14 Physician requirements to prescribe buprenorphine/naloxone are determined at the provincial level, typically by the College of Physicians and Surgeons or an equivalent provincial licensing body. In BC, recommendations regarding buprenorphine/ naloxone administration are under the purview of the CPSBC.12

As fully outlined in Tables 1 and 2 in the appendices, there is considerable variability across Canadian provinces in regulatory and educational requirements for physicians to prescribe buprenorphine/naloxone, and several key issues are evident on review of the national situation. First, prescriber restrictions and requirements have not been systematically described or scrutinized in an evidence-informed manner. Second, in some cases, this has led to provincial program decisions that are based on existing infrastructure (i.e., Provincial Methadone Maintenance Programs), incomplete information, and/or apparent lack of knowledge about relative safety of methadone versus buprenorphine/naloxone. Third, practice and policy for buprenorphine/naloxone administration urgently needs to be updated to reflect the best available science. Prioritizing implementation of evidence-based policy for buprenorphine/naloxone administration in BC will provide patients and families access to a wider range of safe and effective care options, and will have a more meaningful population-level impact on the provincial opioid crisis. With the anticipated changes to buprenorphine/naloxone prescriber restrictions, BC will join several other provinces in Canada that have adopted less restrictive, evidence-based prescribing regulations (Appendix Table 1).

Research evidence clearly supports the role of buprenorphine/naloxone as a first-line treatment option for opioid use disorder. Clinical trials and systematic reviews consistently demonstrate that buprenorphine/naloxone offers comparable treatment outcomes, with fewer side effects and drug interactions, lower health risks of diversion (i.e., use by individuals who do not have a prescription), and significant safety advantages in comparison to methadone.¹⁵ Buprenorphine/ naloxone also demonstrates significant efficacy and favorable safety and tolerability in specific populations, including youth and prescription opioid-dependent individuals.¹⁶ However, buprenorphine/naloxone remains critically underutilized in BC (Figure 2) for a number of reasons, including: a lack of skilled addiction care providers and evidence-based clinical practice guidelines for treatment of opioid use disorder; and traditionally, restrictions on who can prescribe this medication. Historically, only a small subset of BC physicians have been authorized to prescribe buprenorphine/naloxone, as per requirements set by the CPSBC that prescribers must hold a methadone exemption.¹⁷ In coming months, it is expected the requirement that physicians must hold a Section 56 exemption to prescribe buprenorphine/naloxone will be eliminated by the CPSBC. This change is well supported by research evidence, as will be detailed below, as well as considerable public health benefits achieved in other jurisdictions that have adopted buprenorphine/naloxone as a first-line treatment for opioid use disorder.

Figure 2

Number of patients prescribed methadone or buprenorphine in British Columbia, 2010–2014.



Source: BC Opioid Substitution Treatment System Performance Measures, 2013/2014. Office of the Provincial Health Minister, British Columbia Ministry of Health. Released July 2015.

In recent years, concerted efforts have been made to address gaps in the provision of evidencebased treatment and care for substance use disorders, including the ongoing development of comprehensive addiction medicine training programs¹⁸ and the dissemination of the Vancouver Coastal Health/Providence Health Care Guidelines for the Clinical Management of Opioid Use Disorder¹⁹ to clinical sites across the province. As well, as mentioned above, inclusion of buprenorphine/naloxone as a first-line treatment eligible for PharmaCare coverage will improve access and provide individualized options for treating opioid use disorder. These achievements bring focus to remaining barriers within the province, and an opportunity for continued

advancement through upcoming changes to buprenorphine/naloxone prescriber restrictions.

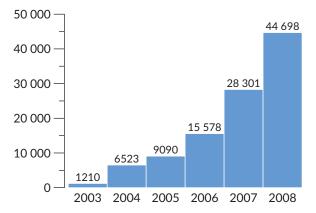
Experience from Other Jurisdictions where Buprenorphine/naloxone is Widely Prescribed. Although not yet widely used across Canada, buprenorphine^{*} use in the US has rapidly expanded over the past decade. Between 2003 and 2008, there was an approximately 35-fold increase in the number of buprenorphine dosage units distributed to US pharmacies (Figure 3).²⁰ In parallel, between 2006 and 2010, there was an approximately fivefold increase in the number of individuals receiving buprenorphine prescriptions on an outpatient basis from primary care or office-based physicians.^{20,21} This transition has largely been driven by "The Drug Addiction Treatment Act" (2000), which enabled all primary care physicians to administer buprenorphine following completion of a short online training course, effectively mobilizing physicians to become active partners in the diagnosis and treatment of opioid use disorder. Increased uptake of buprenorphine for treatment of opioid use disorder has subsequently been associated with considerable public health benefits, in the US and beyond, including: reductions in opioid-related overdose deaths;22,23 decreased illicit opioid and other drug use;24-27 and decreased HIV risk behaviours.28,29 In addition, the ability to treat opioid use disorder in primary care settings has been shown to improve other health outcomes such as the identification and treatment of other chronic medical conditions.30

The emphasis on prioritizing access to buprenorphine for treating opioid use disorder has resulted in considerable health system cost-savings in the US. Studies have demonstrated that over the first six months of treatment, total healthcare costs

^{*} Note: In the US and other jurisdictions, buprenorphine monotherapy (e.g., Subutex[®]) is an approved treatment for opioid addiction, although the combined formulation of buprenorphine/ naloxone is predominantly used for this indication. In this document, the term "buprenorphine" represents data for both products unless otherwise specified. In Canada, buprenorphine monotherapy is not approved for the treatment of opioid addiction and is only available through the Special Access Programme, which provides access to non-marketed drugs for treating patients with serious or life-threatening conditions when conventional therapies have failed, are unsuitable, or unavailable.

Figure 3

Dosage units of buprenorphine per 100,000 population in the United States



Source: DEA's Automation of Reports and Consolidated Orders System (ARCOS). Adapted from Maxwell J, McCance-Katz E. Indicators of buprenorphine and methadone use and abuse: What do we know? The American Journal on Addictions. 2009, 19:73–88

per patient are approximately 1.29 to 1.67 times higher for methadone compared to buprenorphine treatment.^{31,32} Although buprenorphine/naloxone costs more than methadone per unit of drug, significant cost savings can be derived as the requirement for daily dispensation and witnessed ingestion of buprenorphine/naloxone can be eliminated much earlier in the treatment process.³³ On a broader scale, there are significant cost savings associated with buprenorphine/naloxone compared to methadone treatment, including lower ambulatory and emergency department utilization rates,32 fewer hospital admissions (opioid- and non-opioid related)³¹ and reductions in drug-drug interaction management,34 particularly among specific populations such as people living with HIV/AIDS and/or psychiatric comorbidities.35,36 Earlier provision of unmonitored take-home doses also translates to cost savings for patients, with recent studies estimating that patient costs (e.g., transportation, childcare, time and lost productivity) are 1.63 times higher for office-based methadone treatment, and 2.38 times higher for clinic-based methadone treatment, versus officebased buprenorphine treatment.37

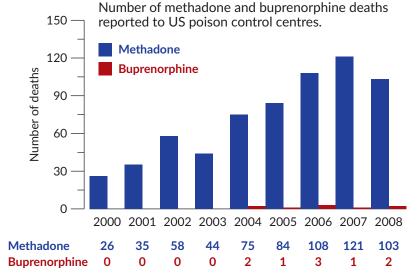
A particularly strong case for the public health benefits of buprenorphine has been made in France, where all registered physicians have been able to prescribe buprenorphine since 1996, without specialist training or licensing requirements. This policy has allowed for low-barrier access to treatment though primary care physicians for approximately 65,000 patients per year nationally, engaging ten times more patients in care than a more restrictive methadone treatment model, which remains an alternative option.²² Overall, approximately 20% of all physicians in France are now prescribing buprenorphine to treat approximately half of the estimated 150,000 opioid users in the country.²² No negative consequences to general population health or safety have been reported; in fact, opioid-related overdose deaths have declined by approximately 80% since 1995.38 These US and European examples raise important questions about the value of tight regulations on prescribing buprenorphine imposed by many countries throughout the world, including Canada.39

Comparative Safety of Methadone and Buprenorphine/naloxone. Although methadone is most commonly used for treating opioid use disorder in BC, safety remains an ongoing public health concern. A provincial review of prescription opioid-related deaths (2004-2013) found that methadone was involved in approximately 25% of opioid overdose fatalities.40 Although provincial data for buprenorphine-related harms are lacking, research from other jurisdictions shows that buprenorphine is a much safer option for treating opioid use disorder, particularly with regards to overdose risk. For example, a recent study in New York City found that detection of buprenorphine in overdose deaths was extremely rare: of 98 unintentional overdose fatalities reported over a five-month period, only two cases (2%) tested positive for buprenorphine, while 20% tested positive for methadone.⁴¹ Similarly, administrative data from the American Association of Poison Control Centers indicates that methadone-related deaths ranged from 26 to 121 between 2000-2008, while the total number of buprenorphine-related deaths ranged from 0 to 3 over the same time period (Figure 4).20,42 Population-based studies (i.e.,

including individuals receiving treatment and the general public) from Australia and the UK have found a four- and six-fold higher risk of fatal overdose for methadone compared to buprenorphine, respectively.^{43,44}

In terms of non-fatal safety risks, a recent US study reported that the number of calls to Poison Control for methadone-related issues was 6.7 times higher than calls for buprenorphine-related issues.42 Of these, nearly double the proportion of methadonerelated calls were associated with major lifethreatening events or events requiring medical attention compared to buprenorphine (46.8%) versus 25.8%).42 Overall, buprenorphinerelated emergency department (ED) visits represent a small proportion of all drugrelated ED visits in the US,45 and are most commonly associated with self-management of withdrawal symptoms,^{46–48} attempts to cease illicit drug use,49 and/or non-serious adverse events shortly after initiation of treatment (e.g., precipitated withdrawal).²¹

Figure 4



Source: National Poison Data System, American Association of Poison Control Centers. Adapted from Maxwell J, McCance-Katz E. Indicators of buprenorphine and methadone use and abuse: What do we know? The American Journal on Addictions. 2009, 19:73-88

These patterns of increased risk with methadone are largely driven by the increased propensity for methadone to trigger respiratory depression. Specifically, methadone doses that exceed the threshold lethal dose for opioid-naïve adults are routinely prescribed to opioid-tolerant patients in opioid agonist treatment programs to adequately control withdrawal symptoms. In comparison, the standard therapeutic buprenorphine/naloxone dose is generally well below the threshold lethal dose and confers a much lower risk of respiratory depression and fatal overdose.⁵⁰ As well, methadone has a higher potential for dangerous interactions with alcohol and many common medications (e.g., antibiotics, antifungals, antidepressants, antiretroviral drugs), as well as increased risk of cardiac arrhythmias as a result of QT prolongation compared to buprenorphine/ naloxone.51 While relatively less common, buprenorphine/naloxone-related overdose fatalities are most often the result of combined use with other central nervous

> system depressants, such as alcohol and benzodiazepines,⁵²⁻⁵⁴ or in the context of intentional self-harm (e.g., suicide attempts where supratherapeutic doses are intentionally taken).⁵⁵ Taken together, this research evidence, and the data depicted in Figure 3 and Figure 4, demonstrate the negligible effects of increased buprenorphine prescribing on rates of mortality and other harms, which must be balanced alongside proven public health benefits, and the relative risks associated with methadone.

> Contributing to safety risks associated with opioid agonist treatment is the potential for diversion, that is, consumption by an individual without a prescription. For example, a UKwide analysis of methadone-related

deaths found that only 36% were among individuals known to be receiving methadone treatment.⁴⁴ This is consistent with reports from Australia, Europe, and the US, which have found that up to 50% of overdose deaths involving methadone are the result of diversion.^{20,43,56} These deaths are a function of the high potency and toxicity of methadone when used outside of a closely monitored setting, as well as its known street value. Although diversion is still a concern with buprenorphine, the fact that it is a partial opioid agonist, and is typically prescribed in Canada in the combined formulation with naloxone, greatly limits risks.⁵⁷

Prior research also indicates that most people who use diverted or street-obtained buprenorphine/ naloxone are opioid users primarily intending to self-medicate withdrawal symptoms rather than seeking euphoric effects.^{46,49,58-60} Strong predictors of buprenorphine/naloxone diversion include inability to access opioid agonist therapy programs and suboptimal dosing for those who are engaged in care.^{21,61-63} Of note, there is no evidence that tighter controls or dose monitoring reduce diversion,²¹ as illustrated by a recent study of all opioid agonist treated patients in Finland that found unsupervised take-home buprenorphine doses were not associated with increased risk of diversion to others.64 In fact, studies have found that patients with prior use of non-prescribed buprenorphine are more likely to enter addiction treatment and have significantly higher odds of remaining in treatment compared to patients who are buprenorphinenaïve upon treatment entry.65 Therefore, efforts to minimize diversion must take this evidence base into consideration and avoid undermining the positive patient and public health benefits that can be gained from expanded treatment access.²¹

Nevertheless, to address concerns regarding buprenorphine/naloxone diversion, there are mechanisms that prescribing physicians can routinely employ, and that regulatory agencies (e.g., CPSBC) can help enforce, including periodic urine drug screens to confirm the presence of buprenorphine and other illicit drugs to assess patient stability, as well as closely monitoring buprenorphine/naloxone use via unannounced pill counts to assess for and limit potential for diversion.

Growing consensus among experts and opinion leaders has culminated in high-level recommendations that buprenorphine/naloxone should be routinely considered as a first-line pharmacotherapy option for opioid use disorder, given its superior safety profile with respect to overdose risk compared to methadone.66-68 This cumulative safety evidence has also led to recent revisions to the buprenorphine/naloxone product monograph that remove the requirement for a two-month period of daily witnessed ingestion, thereby allowing provision of take-home dosing at the judgment of the treating physician (e.g., as soon as the patient has demonstrated clinical stability and ability to safely store buprenorphine/ naloxone at home)? The CPSBC has not yet revised their current recommendation that patients must undergo at least two months of daily witnessed ingestion before take-home doses are permitted. To our knowledge, no other Canadian jurisdiction has enforced take-home dosing restrictions that are inconsistent with the updated Health Canadaapproved product monograph or that mirror those of methadone. In light of this, the CPSBC should consider revising guidance to remove this additional barrier to accessing care, permitting take-home doses at the discretion of the treating physician.

Recommendations. Collective action is needed to address increasing rates of serious harms and deaths associated with opioid use in BC. In light of the public health emergency declaration, it is more important than ever before to accelerate the transfer of research evidence into systemic policy and practice change. BC has shown leadership in several priority areas related to preventing opioid-related harms, including establishment of supervised injection sites and take-home naloxone programs, and the addition of buprenorphine/ naloxone to the PharmaCare formulary. The anticipated deregulation of buprenorphine/ naloxone prescribing provides an opportunity to show continued leadership, through expansion of physician and patient access to a medication with proven safety and effectiveness in treatment of opioid use disorder. To optimize impact, education efforts that build or enhance professional and public knowledge of the comparative risks and benefits of this medication should be prioritized, as should dissemination of evidence-based practice guidelines. As has been demonstrated in other jurisdictions, expanding buprenorphine/naloxone prescribing to primary care and community-based physician practices can lead to considerable public health benefits due to proven safety advantages and lower risks of diversion relative to methadone. Based on the above evidence, it is recommended that:

- Buprenorphine/naloxone should be routinely offered as a first-line pharmacotherapy option (as an alternative to methadone) for opioid use disorder, given its superior safety profile with respect to overdose risk compared to methadone.
- 2. The requirement that BC physicians must hold a methadone exemption in order to prescribe buprenorphine/naloxone should be eliminated. This review fully supports the CPSBC in its deliberations to remove this requirement. In lieu of the methadone exemption, it is recommended that prescribers should be directed to complete the existing online training module on buprenorphine/naloxone prescribing, but not required, in order to optimize the number of prescribing physicians in the province.
- 3. Evidence-based guidelines for buprenorphine/ naloxone treatment that are tailored to clinical practice in BC, such as the Vancouver Coastal Health/Providence Health Care Guideline for the Clinical Management of Opioid Addiction, should be widely disseminated and

implemented to support best practices among new physician prescribers.

- 4. Public and professional education campaigns designed to increase knowledge of buprenorphine/naloxone as a first-line treatment option for opioid use disorder, and the risks and benefits of this medication relative to methadone, should be prioritized.
- 5. Provincial recommendations for take-home dosing of buprenorphine/naloxone should be identical to those on the buprenorphine/ naloxone product monograph: the requirement for a two-month period of daily witnessed ingestion should be removed from provincial OAT program guidelines, allowing provision of take-home dosing at the judgment of the treating physician.
- 6. Research and education aimed at reducing the diversion of opioid agonist therapies should be supported. The development of educational resources and programmatic strategies that support prescribers in assessment, risk reduction and prevention of opioid agonist diversion should be prioritized.

British Columbia is at a critical juncture in our approach to preventing, identifying and treating opioid use disorder. Removing barriers to accessing proven safe and effective treatments is a key component of a broader strategy to combat the opioid crisis. Supporting anticipated regulatory changes and implementing the above recommendations has the potential to substantially improve patient and provider access to muchneeded options for care, and would likely have a meaningful impact on the health and well-being of the many British Columbians affected by opioid use disorders.

Appendix Table 1. Summary of Provincial Regulations^{*} for Buprenorphine/naloxone Administration.

Province	Coverage	Criteria	Prescriber Restrictions
BC ^{12,17,70}	Regular Benefit	First line treatment of opioid dependency in adults	Physicians must have a methadone exemption Note: it is anticipated that this restriction will be removed in mid-2016
Alberta ⁷¹⁻⁷³	Regular Benefit	First line treatment of opioid dependency in adults	No exemption required
Saskatchewan ^{74,75}	Exceptional Status	Prescribed only if methadone is contraindicated, not available or appropriate	Physicians must have a methadone exemption OR have spent a minimum of one day with another physician who has received an exemption from Health Canada to prescribe methadone
Manitoba ^{76,77}	Exception Drug Status	Prescribed only if methadone is contraindicated, not available or appropriate	
Ontario ^{78,79}	Limited Use	Prescribed only if methadone is contraindicated, not available or appropriate	No exemption required
Quebec ⁸⁰⁻⁸²	Exceptional Medication	Prescribed only if methadone is contraindicated, not available or appropriate	No exemption required
New Brunswick ^{83,84}	Special Authorization	Prescribed only if methadone is contraindicated, not available or appropriate	Physicians must have a methadone exemption OR have experience in the treatment of opioid dependence
Nova Scotia ^{85,86}	Standard benefit for adults aged 18–24; Exemption Status coverage required for all adults >24 years	For adults 18–24: first-line treatment for opioid addiction; Adults over 24: Prescribed only if methadone is contraindicated, not available or appropriate	No exemption required
PEI ^{87,88}	Special Authorization	Prescribed only if methadone is contraindicated, not available or appropriate	No exemption required
Newfoundland and Labrador ⁸⁹⁻⁹¹	Special Authorization	Prescribed only if methadone is contraindicated, not available or appropriate	-

*Note: Information was not available for Yukon, Northwest Territories, or Nunavut

Appendix Table 2. Summary of Provincial Educational and Training Requirements* to Prescribe Buprenorphine/naloxone.

Province	Education & Practice Requirements
British Columbia ^{12,17}	• The physician must hold a methadone exemption to prescribe buprenorphine/naloxone for opioid use disorder
	• The current requirements for obtaining an authorization to prescribe methadone for opioid use disorder are:
	 attendance at the Methadone 101 Workshop sponsored by the College familiarization with the Methadone Maintenance Program: Clinical Practice Guideline a preceptorship satisfactory to the Methadone Maintenance Program an acceptable review of your prescription profile from the PharmaNet database an interview with a member of the registrar staff an agreement to undertake a minimum of 12 hours of continuing medical education (CME) in addiction medicine each year an agreement to provide after-hours contact information regarding your methadone maintenance patients an agreement to undergo a practice assessment of your methadone maintenance practice within the first year
	 Additional requirements for obtaining an authorization to prescribe buprenorphine/naloxone for opioid use disorder are:
	 Physicians must have completed the online education module by Schering-Plough Canada available at www.suboxonecme.ca. Completion of this module is based on an honour system, and will not be verified except in unusual circumstances Buprenorphine/naloxone must be prescribed on a duplicate prescription pad
Alberta ^{72,73}	• The physician does not need to hold a methadone exemption to prescribe buprenorphine/naloxone for opioid use disorder
	 The current requirements for obtaining an authorization to prescribe buprenorphine/naloxone for opioid use disorder:
	 Initiation: Completion of accredited buprenorphine course: www.suboxonecme.ca, CAMH Opioid Dependence Treatment Core course or other equivalent course approved by CPSA. Physician must provide confirmation of course completion to the CPSA. Must have experience in treating opioid use disorder: (postgraduate training, ODT experience, professional certification with CSAM/ASAM or equivalent approved by CPSA) Maintenance: Completion of accredited buprenorphine course: www.suboxonecme. ca, the CAMH Opioid Dependence Treatment Core course or other equivalent course approved by CPSA. Physician must provide confirmation of course completion to the CPSA. Must have a relationship with a physician experienced in treating opioid use disorder (postgraduate training, ODT experience, certification with CSAM/ASAM or equivalent approved by CPSA) Temporary prescribing for hospital/incarcerated patients: Temporary buprenorphine prescribing physicians will be permitted to maintain the same buprenorphine dose without completion of a buprenorphine prescribing course. A temporary prescribing physician must consult with a physician experienced in the treatment of opioid dependency for any dose changes. Must have a relationship with physician experienced in the treatment of opioid dependency for any dose changes. Must have a relationship with physician experienced in the physician experienced in the physician experienced in the treatment of opioid dependency for any dose changes. Must have a relationship with physician experienced in the treatment of opioid dependency for any dose changes. Must have a relationship with physician experienced in the physician

Saskatchewan ⁷⁵	• The physician must hold a methadone exemption to prescribe buprenorphine/naloxone for opioid use disorder or have spent a minimum of one day with another physician who has received an exemption from Health Canada to prescribe methadone.		
	 The current requirements for obtaining an authorization to prescribe methadone for opioid use disorder are: Physician must have license to practice medicine in Saskatchewan Initiation: Completion of MMT workshop/course recognized by CPSS Direct training (2 days) with experienced, CPSS approved initiating physician Documentation of clinical competence College approved mentorship for first two years of practice Must pursue ongoing education relevant to MMT Must access PIP viewer prescribing database An interview with a member of the registrar staff Must have access to laboratory services and a pharmacy Must be limited to 50 patients until first audit Maintenance: Completion of MMT workshop/course recognized by the CPSS Must have an ongoing association with experienced initiating physician Must access PIP viewer prescribing database An interview with a member of the registrar staff Must be limited to 50 patients until first audit Maintenance: Completion of MMT workshop/course recognized by the CPSS Must have an ongoing association with experienced initiating physician Must access PIP viewer prescribing database An interview with a member of the registrar staff Temporary Prescribing: Must consult CPSS if initiating physician is not available Must only prescribe for duration of patients hospital admission Must not prescribe carried doses Prior to patient discharge, temporary prescribing physician must collaborate with initiating or maintaining physician. 		
	 Additional requirements for prescribing buprenorphine/naloxone for opioid use disorder include: Completion of the online education module – www.suboxonecme.ca Physicians must have training and interest in addiction medicine Buprenorphine/naloxone prescriptions must be written on the physician's personalized prescription pad/CPSS approved electronic prescribing 		
Manitoba ⁷⁶	 The physician must hold a methadone exemption to prescribe buprenorphine/naloxone for opioid use disorder The current requirements for obtaining an authorization to prescribe methadone for opioid use disorder are: Completion of CAMH Course: Opioid Dependence Treatment Core Course A one day clinical observership of opioid dependency practice Completion of several supervised shifts in a methadone/buprenorphine clinic (minimum of 4 half days) Alternatively, extensive experience in methadone/buprenorphine addiction practice in another province Additional Requirements for prescribing buprenorphine/naloxone for opioid use disorder include: Completion of CAMH course: Buprenorphine-Assisted Treatment of Opioid Dependence: An Online Course for Front-Line Clinicians Completion of buprenorphine/naloxone Education Program Online course www.suboxonecme.ca 		

Ontario ⁷⁸	 The physician does not need to hold a methadone exemption to prescribe buprenorphine/naloxone for opioid use disorder The current requirements for obtaining an authorization to prescribe buprenorphine/naloxone for opioid use disorder are: Completion of CAMH course: Opioid Dependence Treatment Core course. Completion of CAMH course: Buprenorphine-Assisted Treatment of Opioid Dependence: An Online Course for Front-Line Clinicians Completion of buprenorphine/naloxone Education Program Online course — www.suboxonecme.ca A one day clinical observership of an opioid dependency practice
Quebec ^{80,81}	buprenorphine/naloxone for opioid use disorder
New Brunswick ⁸³	opioid use disorder to prescribe buprenorphine/naloxone for opioid use disorder
Nova Scotia ⁸⁵	 The physician does not need to hold a methadone exemption to prescribe buprenorphine/naloxone for opioid use disorder The current requirements for obtaining an authorization to prescribe buprenorphine/naloxone for opioid use disorder are: Completion of CAMH online buprenorphine course Must be prescribed using a PMP duplicate prescription pad

PEI ^{87,88}	 The physician does not need to hold a methadone exemption to prescribe buprenorphine/naloxone for opioid use disorder 		
	The current requirements for obtaining an authorization to prescribe buprenorphine/naloxone for opioid use disorder are:		
	 An unrestricted license for independent practice in the province of Prince Edward Island, in good standing with no relevant conditions or restrictions 		
	 No current investigations with regard to prescribing opioids or record keeping 		
	 No previous findings of professional misconduct or previous legal findings with regard to opioids or record keeping 		
	 Ongoing education relevant to prescribing buprenorphine for opioid dependency including: 		
	 Completion of Buprenorphine/naloxone Education Program available online – www.suboxonecme.ca 		
	 Completion of a recognized course on the fundamentals of addiction medicine within first two years of commencing prescribing 		
	 Completion of a minimum of 20 hours of formal CME in some aspect of addiction medicine every five years 		
	 Completion with signature of form entitled Commitment by Physicians who Undertake Buprenorphine Treatment for Opioid Dependency 		
Newfoundland and Labrador ^{89,90}	• The physician must have a methadone exemption to prescribe buprenorphine/naloxone for opioid use disorder		
	 The current requirements for obtaining an authorization to prescribe buprenorphine/naloxone for opioid use disorder are: 		
	 Obtain Methadone Exemption according to Section 56 of Controlled Drugs and Substances Act 		
	 Completion of Buprenorphine prescription training program approved by college Participation in continuing medical education in opioid-dependence treatment Completion of minimum one-day clinical observership at the Opioid Treatment Centre in province 		

*Note: Information was not available for Yukon, Northwest Territories, or Nunavut

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Authors and Contributors

Keith Ahamad, MD, CCFP, CISAM, Dip ABAM

Family and Addiction Medicine Physician, Providence Health Care / Vancouver Coastal Health Research Scientist, BC Centre for Excellence in HIV/AIDS Clinical Assistant Professor, Faculty of Medicine, UBC

Thomas Kerr, PhD

Director, Urban Health Research Initiative, BC Centre for Excellence in HIV/AIDS Professor, Faculty of Medicine, UBC

Seonaid Nolan, MD, FRCPC, Dip ABAM

Internal Medicine and Addiction Medicine Physician, Providence Health Care Research Scientist, Urban Health Research Initiative, BC Centre for Excellence in HIV/AIDS Clinical Assistant Professor, Faculty of Medicine, UBC

Evan Wood, MD, PhD, ABIM, FRCPC

Director, Urban Health Research Initiative, BC Centre for Excellence in HIV/AIDS Professor of Medicine, Canada Research Chair in Inner City Medicine, UBC Medical Director, Community Addiction Services, Vancouver Coastal Health / Providence Health Care Principal Investigator, British Columbia Node of the Canadian Research Initiative in Substance Misuse (CRISM)

Conflicts of Interest

The authors of this report have no conflicts of interest to declare.

Specifically, the authors confirm that they have no affiliations with or involvement in any private corporation or entity, and have no financial interests (i.e., have not received any honoraria; educational grants; membership, employment, consultancies, stock ownership, or other equity interest; expert testimony or patent-licensing arrangements) in any private corporation or entity that would unduly influence the content or recommendations made in this report.

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