College of Physicians and Surgeons of British Columbia

Methadone and Buprenorphine: Clinical Practice Guideline for Opioid Use Disorder

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CONTENTS

PREFACE

The College of Physicians and Surgeons of British Columbia, in partnership and under contract with the Ministry of Health, operationalizes aspects of the Methadone Maintenance Program in British Columbia, including the provision of guidelines.

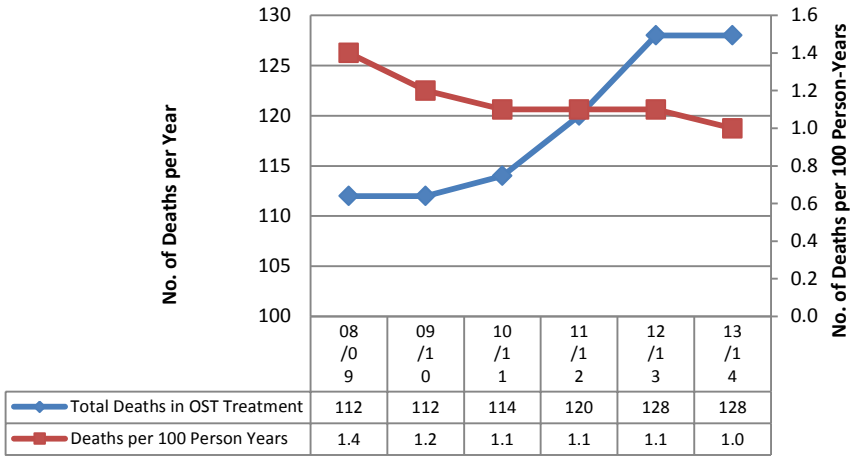
These guidelines reflect the expert advice of the consultants and panel members appointed by the College, adhere to current regulations, are based on current medical evidence, and are intended for prescribers of methadone or buprenorphine in British Columbia, in the interest of promoting positive patient health outcomes and public health and safety.

*A **guideline** reflects a recommended course of action established based on the values, principles and duties of the medical profession. Physicians may exercise reasonable discretion in their decision to act on the guidance provided, but should support a decision to follow a different action with a comprehensively documented rationale.*

For the purposes of this document, the term buprenorphine is used to represent any formulation containing buprenorphine for use in treatment of opioid use disorder, including the combination of buprenorphine-naloxone.

The benefits of opioid substitution treatment extend beyond reduction of illicit or prescription drug misuse. Engaging patients in treatment can facilitate harm reduction outcomes that may include: decreased overdoses (which can lead to hospitalization or death); reduced high-risk behaviours; addressing concurrent disorders; improved health; and reestablishment of normal socioeconomic and family functioning. For the first time in several years, the all-cause mortality rate during medication-assisted treatment for opioid use disorder did not increase from 2012/13 to 2013/14, while the number of patients enrolled in treatment increased.

Figure 1: All-cause Mortality During Opioid Substitution Treatment, by Fiscal Year, BC, 2008/2009 to 2013/2014



	08/09	09/10	10/11	11/12	12/13	13/14
Total Deaths in OST Treatment	112	112	114	120	128	128
Deaths per 100 Person Years	1.4	1.2	1.1	1.1	1.1	1.0

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Methadone Maintenance Program (MMP)

The objective of the MMP is to assist physicians in safely and effectively prescribing methadone or buprenorphine as medication-assisted treatments for opioid use disorders (OUD).

The MMP is contracted by the Ministry of Health to provide the following:

- guidelines for safe and effective prescribing of methadone or buprenorphine for OUD
- education including workshops on prescribing methadone or buprenorphine for OUD
- preceptorships for physicians who wish to prescribe methadone or buprenorphine for OUD
- practice assessments of the physicians who are authorized to prescribe methadone or who are prescribing buprenorphine
- recommendations to the federal Ministry of Health regarding methadone authorizations
- maintaining a central registry of physicians who are exempted by Health Canada to prescribe methadone

This guideline addresses the prescribing of methadone and buprenorphine for the treatment for OUD — physicians prescribing methadone for analgesia (both for palliative and chronic non-cancer pain) should refer to the handbook *Methadone for Analgesia Guidelines*.

INTRODUCTION

1. The History of Methadone

Methadone was discovered in 1938 by two German scientists, Max Bockmühl and Gustav Ehrhart, and was patented in September 1941. Bockmühl and Ehrhart were attempting to find a gastrointestinal tract antispasmodic and analgesic which would be structurally dissimilar to morphine, non-addictive, and would escape the strict legal controls placed on opioids at that time. In 1947, Harris Isbell and his colleagues, who had been experimenting extensively with methadone, discovered that methadone was beneficial in the treatment of opiate-dependent patients.[1]

Several studies from the United Kingdom in the 1940s described methadone's efficacy in reducing heroin withdrawal symptoms. Ingeborg Paulus and Dr. Robert Halliday, working with the Narcotic Addiction Foundation in Vancouver, established the first methadone maintenance treatment program in the world and published their findings in the *Canadian Medical Association Journal* in 1967.[2] In the United States, Dr. Vincent Dole and Dr. Marie Nyswander confirmed the feasibility of using methadone as a maintenance medication for heroin dependence.[3] Since then, many other studies have shown the effectiveness of using methadone as a maintenance medication for opioid use disorder. These studies demonstrate a three- to four-fold increase in death rates in patients discontinuing methadone maintenance treatment.[4,5] In addition to physical, mental and social health benefits, studies have consistently shown that risk of blood-borne pathogen transmission is significantly reduced by participation in methadone maintenance treatment, even in patients failing total abstinence from illicit substances.[6]

1.2 Buprenorphine

Buprenorphine was first synthesized in the 1960s[7] from thebaine, a chemical naturally derived from the opium poppy. It was initially approved for medical use as an intravenous analgesic by the United Kingdom in 1979, and by the United States Food and Drug Administration in 1985. The use of buprenorphine as a treatment for opioid addiction was first proposed in 1978.[8] In 1985, a report on the

[1] Isbell H, Wikler A, Eddy NB, Wilson JL, Moran CF. Tolerance and addiction liability of 6-dimethylamino-4-4-diphenyl- hyptanone-3 (methadon). J Am Med Assoc. 1947 Dec 6;135(14):888–94.
[2] Paulus I, Halliday R. Rehabilitation and the narcotic addict: results of a comparative methadone withdrawal program. Can Med Assoc J. 1967 Mar 18;96(11):655-9.
[3] Dole VP, Nyswander ME. A medical treatment for diacetylmorphine (heroin) addiction: a clinical trial with methadone hydrochloride J Am Med Assoc. 1965;193:646-50.
[4] Bell J and Zador D. A risk-benefit analysis of methadone maintenance treatment. Drug Saf, 2000 Mar; 22(3):179-90.
[5] Humeniuk R, Ali R, White J, Hall W, Farrell M. Proceedings of expert workshop on the induction and stabilisation of patients onto methadone. Monograph 39. Adelaide: Commonwealth Department of Health and Aged Care; 2000.
[6] Leshner AI. Science-based views of drug addiction and treatment. JAMA. 1999;282(14):1314–16.
[7] Bentley KW. (Manske RH, Holmes HL, Eds). The Alkaloids, Chemistry & Physiology, Vol. XIII, Academic Press,1971, pp 3-163
[8] Jasinski DR, Pevnick JS, Griffith JD. Human pharmacology and abuse potential of the analgesic buprenorphine. Arch Gen Psychiatry 1978;35:501-51

use of sublingual (SL) buprenorphine in the treatment of 65 heroin-addicted individuals in Belgium was published.[9] In 1988, a 30-day sublingual buprenorphine outpatient detoxification from opioid dependence was reported,[10] and in 1992 a randomized, double-blinded study compared SL buprenorphine to methadone for the treatment of opioid dependence.[11] Buprenorphine was approved for the treatment of opioid addiction by France in 1996, the US in 2002, and Canada in 2007. In 2010, a transdermal formulation of buprenorphine was approved for use in Canada as an analgesic.

2. Authorization to Prescribe Methadone and Buprenorphine Maintenance Treatment (MBMT)

2.1 Methadone

Methadone is a controlled drug under section 56 of the *Controlled Drugs and Substances Act*. Physicians who wish to prescribe methadone in Canada require authorization in the form of an exemption from the federal minister of health, which is obtained through the College of Physicians and Surgeons of BC.

The words "exemption" and "authorization" both refer to the exemption which is granted under section 56 of the *Controlled Drugs and Substances Act* and which authorizes a physician to prescribe methadone.

Physicians can apply for one of three types of authorizations to prescribe methadone for opioid use disorder: full, temporary or hospitalist.

2.1.1 Full Authorization

The College will recommend a full authorization to Health Canada only after the following requirements have been satisfactorily fulfilled:

- a completed Application for Authorization to Prescribe Methadone in the Treatment of Opioid Use Disorder from the College website
- attendance at the Methadone 101 Workshop sponsored by the College, or equivalent education
- completed review of the *Methadone and Buprenorphine: Clinical Practice Guideline*
- a preceptorship satisfactory to the MMP
- an acceptable review of the practitioner prescribing profile from the PharmaNet database

Contact the Methadone Maintenance Program for a list of approved preceptors.

[9] Reisinger M. Buprenorphine as new treatment for heroin dependence. Drug Alcohol Depend 1985;16:257-262.
[10] Kosten TR, Kleber HD. Buprenorphine detoxification from opioid dependence: a pilot study. Life Sciences 1988;42:635-641.
[11] Johnson RE, Jaffe JH, Fudala PJ. A controlled trial of buprenorphine treatment for opioid dependence. JAMA 1992;267:2750-2755.

- an interview with a member of the registrar staff
- a commitment to undertake a minimum of 12 hours of continuing medical education (CME) in addiction medicine each year
- a commitment to participate in practice assessments of their methadone/buprenorphine maintenance practices

The initial authorization is granted for one year. Continued support for this authorization is contingent upon satisfactory practice assessments.

2.1.2 Temporary Authorization

A temporary authorization to prescribe methadone for up to 60 days can be obtained in the following circumstances:

- locum replacement of another authorized physician: Temporary Authorization to Prescribe Methadone as a Locum in a Clinic or Correctional Centre (physician-specific)
- continuation of methadone prescribing for patients in hospital: Temporary Authorization to Prescribe Methadone in a Hospital (patient-specific)

Temporary authorizations do not allow physicians to initiate patients on methadone treatment for OUD, or increase their dose, without first consulting a physician with a full authorization. This may be their community prescriber, if available, another physician with a full authorization, or addiction specialty support through the RACE line (http://www.raceconnect.ca/specialty-selection-menu/). Temporary authorizations are not required to prescribe buprenorphine; however, before initiation of inpatients on either methadone or buprenorphine, it is important to identify and communicate with a physician in the community willing to prescribe for the patient upon discharge.

2.1.3 Hospitalist Authorization

The hospitalist authorization is a dual authorization to prescribe methadone for analgesia and OUD. This authorization is applicable to inpatients and may include a discharge prescription. For continuity of care, liaison with a community methadone prescriber must be arranged prior to the patient's discharge. Please also refer to Hospitalized Patients.

Physicians caring for methadone patients in a hospital setting may apply for a hospitalist methadone authorization after satisfactorily fulfilling the following requirements:

- a completed Application for Authorization to Prescribe Methadone as a Hospitalist
- attendance at the Methadone 101/Hospitalist Workshop sponsored by the College
- completed review of the *Methadone and Buprenorphine: Clinical Practice Guideline* and *Methadone for Analgesia Guidelines*
- an acceptable review of your prescription profile from the PharmaNet database

2.2 Buprenorphine

As of July 22, 2016, a federal authorization is not required to prescribe buprenorphine in British Columbia. Before prescribing more than short-term transitional treatment (no more than one week) physicians should do the following:

1. complete a recognized buprenorphine education program (www.suboxonecme.ca)
2. prescribe buprenorphine dispensed daily under the supervision of a healthcare professional (daily witnessed ingestion) until the patient has sufficient clinical stability and is able to safely store buprenorphine take-home doses
3. be familiar with and follow the *Methadone and Buprenorphine: Clinical Practice Guideline* and the professional standard on *Safe Prescribing of Drugs with Potential for Misuse/Diversion*, including:
    a. reviewing a patient's current medication profile through PharmaNet (e.g. access in office, or via pharmacist communication)
    b. implementing urine drug testing (UDT) protocol which involves supervised random testing
    (**Note**: buprenorphine may not be detected on standard UDT and may need to be ordered separately)
    c. documenting discussion of availability and benefits of biopsychosocial support

Physicians are advised to consult more experienced prescribers of buprenorphine when necessary to enhance their knowledge and ensure patient safety during induction or reinduction after missed doses. It is strongly recommended (but no longer mandatory) that buprenorphine prescribers obtain their federal authorization to prescribe methadone for opioid use disorder in order to be able to offer their patients a broader spectrum of pharmacologic treatment options.

Buprenorphine-naloxone is currently contraindicated in pregnancy; however, physicians may contact Health Canada's Special Access Programme to obtain authorization for the buprenorphine-only product.

3. Pharmacology of Methadone

Methadone is a long-acting synthetic opioid which as an oral formulation is effective in treating opioid dependence. It is primarily a mu (μ) opioid receptor agonist and when administered in an adequate dose, it will prevent opioid withdrawal, reduce opioid craving and mitigate the euphoric effects of opioids such as heroin.

3.1 Absorption

- Oral methadone is 80 to 95% bioavailable compared to only 30% for oral morphine.
- Methadone is rapidly absorbed following oral administration and serum levels are detectable 30 minutes post dose.

3.2 Duration of Action/Metabolism

- The time to peak plasma concentration and peak clinical effect is four hours (range of two to six hours).
- The plasma half-life (t ½) averages 24 to 36 hours at steady state, but ranges from four to 90 hours.
- As a result of its long half-life, methadone may accumulate, leading to sedation and respiratory depression.
- **It takes four to five days (if using t ½ of 24 hours) for methadone plasma levels to reach steady state after each dose change.**
- Methadone metabolism is primarily a function of liver enzyme activity involving cytochrome P450 isoforms. There are many substances that interact by inducing, inhibiting or acting as a substrate for these enzymes. This can result in clinically significant drug interactions. Genetic, physiologic and environmental factors can also act on these enzymes, leading to a high degree of variation of individual methadone responsiveness.
- Methadone is primarily excreted as an inactive metabolite (10% as unchanged methadone) primarily in urine and feces. Compromised renal function does not preclude the use of methadone, and the dosage does not need to be adjusted for patients on dialysis.
- Elimination half-life is approximately 22 hours, but ranges from five hours to 130 hours.

A list of medications metabolized by cytochrome P450 3A4 is available here.

3.3 Tolerance

- Cross-tolerance between methadone and other opioids is unpredictable.
- Tolerance to the various effects of methadone develops at different rates. Tolerance to the euphoric effects of methadone develops quickly and may be interpreted by patients as being due to an inadequate dose. Tolerance to respiratory depression is less rapid in onset and tolerance to the autonomic side effects is the slowest.
- Tolerance is lost in as little as three days.
- Methadone is potentially lethal and the risk of toxicity is increased by concomitant ingestion of alcohol and sedative-hypnotics such as benzodiazepines and Z drugs.

4. Pharmacology of Buprenorphine-naloxone

Buprenorphine-naloxone (Suboxone®, generics) combines buprenorphine, a long-acting synthetic opioid and partial mu (μ) opioid receptor agonist, and naloxone, an opioid antagonist whose inclusion is intended to limit tampering, non-medical injection, and the potential for diversion. When administered sublingually in an adequate dose, it will prevent opioid withdrawal, reduce opioid craving and block the

euphoric effects of opioids such as heroin. The naloxone component of buprenorphine-naloxone has limited sublingual and oral bioavailability and is inactive when buprenorphine-naloxone is taken as prescribed.

Unlike more typical full opioid agonists (such as morphine and hydromorphone), the opioid effect of buprenorphine plateaus (or reaches a "ceiling") as the dose increases further within its usual therapeutic dose range. It is believed that this limit to the opioid effect of buprenorphine results in a lower risk of over-sedation and accidental overdose compared to full opioid agonists.

Buprenorphine has a much higher binding affinity and lower intrinsic activity compared to most opioid agonists. As a result, buprenorphine can displace most other opioids from opioid receptors. For example, buprenorphine will displace fentanyl from opioid receptors.[12]

This explains buprenorphine's ability to precipitate opioid withdrawal in individuals whose tolerance to opioids exceeds buprenorphine's maximal opioid effect. The maximal agonist effect of buprenorphine is equivalent to approximately 30 to 60 mg of methadone, or to 30 mg of morphine subcutaneously four times daily. Buprenorphine also has a much slower rate of association with, and dissociation from, opioid receptors. As a result, while patients are taking buprenorphine, the addition of other opioids **may** be ineffective in terms of euphoria (a desired effect) and analgesia (an undesired effect).[13] Buprenorphine's higher binding affinity and slower dissociation from opioid receptors also makes it more resistant to displacement by naloxone. Compared to fentanyl, it is 40 times more resistant to reversal by naloxone. Compared to typical opioid agonists, buprenorphine is a kappa receptor antagonist, and has a lower binding affinity to delta opioid receptors. It is hypothesized that buprenorphine's kappa receptor antagonist action may give buprenorphine anti-hyperalgesic properties, while full opioid agonists may actually promote hyperalgesia.[14]

4.1 Absorption

- Buprenorphine is well absorbed sublingually, but has poor bioavailability when orally ingested due to first-pass hepatic metabolism. It has high lipid solubility.

4.2 Duration of Action/Metabolism

- Peak concentration is reached 90 to 100 minutes after sublingual administration.
- The half-life after sublingual administration is 29 to 37 hours.
- Metabolism occurs in the small intestine and liver via N-dealkylation and glucuronidation, leading to three major metabolites: buprenorphine glucuronide, N-dealkylbuprenorphine, and

[12] Boas RA, Villiger JW. Clinical actions of fentanyl and buprenorphine. Br J Anaesth 1985;57:192-196.
[13] Marcucci C, Fudin J, Thomas P, Sandson NB, Welsh C. A new pattern of buprenorphine misuse may complicate perioperative pain control. Anesthesia and Analgesia 2009;108(6):1996-1997.
[14] Pergolizzi J, Aloisi AM, Dahan A, Filitz J, Langford R, Likar R, Mercadante S, Morlion B, Raffa RB, Sabatowski R, Sacerdote P, Torrres LM, Weinbroum AA. Current knowledge of buprenorphine and its unique pharmacologic profile. Pain Practice 2010;10(5):428-50.

norbuprenorphine glucuronide. Of these, only norbuprenorphine is biologically active; however, its clinical importance is questionable as it does not readily cross the blood brain barrier.

- First-pass hepatic metabolism, enterohepatic cycling, and biliary excretion occur. Fifity to 71% of buprenorphine is eliminated in the stool, and 10 to 17% is excreted by the kidneys.[15]

4.3 Formulations

- In Canada, buprenorphine for the treatment of addiction is available as a sublingual tablet that is formulated with naloxone in a 4:1 ratio (2 mg buprenorphine/0.5 mg naloxone and 8 mg buprenorphine/2 mg naloxone), under the trade name Suboxone®. The incorporation of naloxone into the sublingual tablet is intended to discourage injection misuse of the tablet preparation. When taken properly, the buprenorphine is absorbed sublingually, but the naloxone is not well absorbed and produces no clinical effect.
- Buprenorphine is also available as a sublingual tablet without naloxone under the trade name Subutex®, but its use is limited to pregnant women. In order to obtain Subutex®, the physician must submit an application to Health Canada's Special Access Programme.
- In Canada, buprenorphine for use as an analgesic is available as a transdermal patch.
- Outside of Canada, other preparations of buprenorphine are available or in development including quick dissolving sublingual tablets, sublingual film, depot injectable, or slow release implant (for the treatment of opioid use disorder), as well as intravenous preparations (for analgesia).

[15] Budd K, Raffa RB, ed. Buprenorphine-The unique opioid analgesic. Georg Thieme Verlag KG 2005, pp 3-21.

ADMISSION TO THE METHADONE MAINTENANCE PROGRAM

1. Criteria for Admission to the Methadone Maintenance Program

As of July 22, 2016, physicians are no longer required to register patients with the MMP. Before initiating methadone or buprenorphine maintenance treatment, the physician must document that the patient meets the following criteria:

- DSM-5 criteria for opioid use disorder and/or DSM-IV-TR criteria for opioid dependence
- comprehensive evaluation to determine the risks and benefits of pharmacologic vs other treatment options
- documented goals of treatment
- informed of all other treatment options for OUD so that their decision to start MBMT is based on valid informed consent

These forms are available for your use:

- MMP Patient Assessment Form
- Methadone Maintenance Treatment Agreement and Consent
- Family Physician Notification

Methadone and buprenorphine prescribers should not hesitate to seek a second opinion when dealing with difficult management problems such as patients with chronic pain, adolescents, pregnant patients and patients with polydrug dependence. See Special Populations for more information.

2. DSM-5 Opioid Use Disorder and DSM-IV-TR Diagnostic Criteria for Opioid Dependence

DSM 5 opioid use disorder is defined as follows:

A problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least two (or more) of the following, occurring within a 12-month period:

Note: Severity	Mild:	Presence of 2-3 symptoms
	Moderate:	Presence of 4-5 symptoms
	Severe:	Presence of 6 or more symptoms

1. Substance is often taken in larger amounts or over a longer period than was intended
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use
3. A great deal of time is spent in activities necessary to obtain the opioid, use the opioid or recover from its effects
4. Craving, or a strong desire or urge to use opioids
5. Recurrent opioid use resulting in failure to fulfill major role obligations at work, school or home
6. Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids
7. Important social, occupational, or recreational activities are given up or reduced because of opioid use
8. Recurrent opioid use in situations in which it is physically hazardous
9. Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been cause or exacerbated by the substance
10. Tolerance, as defined by either of the following:
    a. a need for markedly increased amounts of opioids to achieve intoxication or desired effect
    b. a markedly diminished effect with continued use of the same amount of the opioid; however, this criterion is not considered to be met for those taking opioids solely under appropriate medical supervision
11. Withdrawal, as manifested by either of the following:
    a. the characteristic opioid withdrawal syndrome
    b. opioids (or closely related substance) is taken to relieve or avoid withdrawal symptoms

DSM-IV-TR opioid dependence, as a type of substance dependence, is defined as follows:

A **maladaptive pattern of substance use**, leading to clinically significant impairment or distress, **as manifested by** three (or more) of the following, occurring at any time in the same 12-month period:

1. Tolerance, as defined by either of the following:
    a. a need for markedly increased amounts of the substance to achieve intoxication or desired effect
    or
    b. markedly diminished effect with continued use of the same amount of the substance
2. Withdrawal, as manifested by either of the following:
    a. the characteristic withdrawal syndrome for the substance (refer to criteria A and B of the criteria sets for withdrawal from the specific substances)
    or
    b. the same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms
3. The substance is often taken in larger amounts or over a longer period than was intended
4. There is a persistent desire or unsuccessful efforts to cut down or control substance use
5. A great deal of time is spent in activities necessary to obtain the substance (e.g., visiting multiple doctors or driving long distances), use the substance (e.g., chain-smoking), or recover from its effects
6. Important social, occupational, or recreational activities are given up or reduced because of substance use
7. The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance (e.g. current cocaine use despite recognition of cocaine-induced depression, or continued drinking despite recognition that an ulcer was made worse by alcohol consumption)

3. Treatment Considerations

It is recommended that MBMT be part of a spectrum of treatment focused on improving health and social outcomes. Because many MBMT patients are polysubstance dependent, it is important for physicians prescribing methadone or buprenorphine to be aware of, and familiar with, a broad range of other treatment resources. The problematic use of one substance places the individual at risk of having problems with others (including process addictions)—this is often termed cross-addiction. It is current expert opinion that MBMT is compatible with abstinence-based treatment programs. Lifestyle modification and biopsychosocial support are important aspects of the treatment of substance use disorders; however, patient refusal or reluctance to engage should not preclude access to MBMT.

3.1 Withdrawal Management

Withdrawal management, or detoxification, refers to the management of substance withdrawal in order to reduce severity of symptoms. Many MBMT patients are also dependent on other substances, and these dependencies must be addressed in order to achieve long-term stability. In-patient or outpatient withdrawal management for other psychoactive substances such as alcohol, sedative-hypnotics or stimulants should be offered concurrently.

Subsequent transition to long-term treatment is recommended, to reduce risk of relapse, overdose and blood-borne pathogen transmission. When the physical dependence subsides, patients are at high risk for relapse and should be monitored closely. Psychological and social factors are often powerful stimuli for ongoing use. Patients should be advised on post-acute withdrawal syndrome and emotional distress associated with prolonged withdrawal. Naltrexone may be provided as a deterrent to opioid use and to reduce the risk of overdose. Physicians should be familiar with naltrexone treatment for opioid use disorder prior to initiating such therapy.

3.2 Outpatient and Day Treatment Programs

Most health authorities, community substance use services, employee assistance programs and private service providers offer a range of outpatient and day treatment programs. Physicians prescribing methadone or buprenorphine must be familiar with outpatient programs in their respective communities and build relationships with other care providers. Successful treatment for opioid and other addictions may include biopsychosocial supports, together with regular interactions with physicians.

3.3 Residential and Support Recovery Programs

Residential and support recovery programs vary in structure, length and mandate. Physicians practising addiction medicine must be familiar with the philosophy, entrance criteria and treatment objectives of available residential programs. Many programs accept patients in the MMP and offer patients with addictions a substantial opportunity for behavioural change and long-term abstinence. These programs offer safe, supportive housing as well as aftercare for patients who have completed detoxification or who are on MBMT.

3.4 Mutual Support Groups

Mutual support groups such as Narcotics Anonymous, Methadone Anonymous, Alcoholics Anonymous, SMART and 16-Steps, are generally accessible, promote accountability, and may provide continuing support for behavioural changes that are part of the recovery process.

3.5 Family Involvement

Engaging significant others or family members is beneficial to supporting the patient and increasing their chances of successful outcomes. Family members can provide information not always gleaned from regular interaction with the patient (while considering privacy legislation), and they can be educated to support the patient throughout the recovery process. Family members may want to consider getting a take-home naloxone kit, in case the patient experiences an opioid overdose due to either their methadone/buprenorphine, or a relapse to illicit opioid use. In March 2016, naloxone was moved to Schedule II status in BC, which means it can be obtained without a prescription in the pharmacy. Naloxone is kept behind the pharmacy counter, to allow pharmacists to counsel purchasers on ways to recognize overdose, and how to administer naloxone in those situations. Collaboration with the health-care team in all stages of care further strengthens the trust relationship between all parties, by allowing consideration of values and beliefs in treating the patient with dignity.

3.6 Mental Health Services

Physicians treating substance use disorders must be familiar with the identification and management of common mental illness and be aware of treatment resources in their community. Co-morbidity of psychiatric disorders such as mood disorders, anxiety disorders and post-traumatic stress disorder is prevalent in this population. It is the current standard of care that mental illness and addiction be treated concurrently. For more information, see Mental Health – Concurrent Disorders.

COMMUNICATION AND ADMINISTRATIVE PROCESS CHANGES

It is expected that prescribers of methadone or buprenorphine adhere to the following best practices:

1. Use of PharmaNet

PharmaNet must be reviewed at each visit. Medication reconciliation is necessary at any stage of care transition. Communication with the patient is essential to determine the best possible medication history, including non-prescription drugs and natural products. PharmaNet review should be clearly documented in the patients chart. The College requires that all methadone clinics have on-site PharmaNet access.

2. Communications with Prescribers and Pharmacies

When there is shared care among a number of prescribers, it is essential that there is regular communication between the prescribers to include discussion of each prescriber's scope and responsibility to ensure a coherent care plan for their mutual patient. The communication should be recorded in the patient's chart. Communication with the pharmacy and pharmacists is also encouraged as they often provide important information to better inform care decisions.

3. Single Prescriber Best Practice

Confusion can be created when there are multiple prescribers. While it is not always possible, it is recommended that there should be a single prescriber or clinic. A single pharmacy for dispensing, of the patient's choice and acceptable to the prescriber, should also be considered.

ASSESSMENT FOR INITIATION

The treating physician is responsible for determining patient diagnosis and suitability, appropriate dosing, monitoring the patient, and documenting progress.

The Methadone Maintenance Program provides the following forms for your use:

- MMP Patient Assessment Form
- Methadone Maintenance Treatment Agreement and Consent
- Family Physician Notification

1. Assessment Checklist

Assessment of substance-dependent patients must include the following:

1. complete medical history, including HIV, hepatitis, psychiatric history and current mental health status (including suicidal ideation)
2. chronological substance-use history (including alcohol and tobacco), confirming the DSM diagnosis with documentation of opioid use disorder, other substance use disorder, and process addictions diagnoses
3. family history including history of problematic substance use, addiction treatment history and response
4. biopsychosocial assessment with relevant information regarding the patient's current and past social situation, including supports (e.g. family, clergy, friends), stressors (e.g. legal, employment, financial, children at risk, partner's drug use and housing) and high–risk behaviours (e.g. needle sharing, involvement in sex trade)
5. complete physical examination with special attention to signs of opioid withdrawal, needle tracks, abscesses, malnutrition, jaundice and hepatosplenomegaly (or other stigmata of liver disease)
6. documentation of urine drug test (UDT)
7. laboratory assessment which includes the following:
    - CBC
    - Liver and kidney function panels
    - HIV and hepatitis A, B and C serology
    - Syphilis, chlamydia and gonorrhea serology
    - TB testing, when appropriate
    - Pregnancy test, on all women of child-bearing age
    - ECG if indicated
8. documented communication with the patient's prior methadone prescriber and family physician

9. documented review of the PharmaNet prescription profile, including consideration of drug interactions with current medication regimen, especially drugs that prolong QTc interval or cause sedation/respiratory depression
10. documented treatment goals and plans, with a signed treatment agreement
11. documented discussion of safe storage of prescribed medication (e.g. lock box, safe)

2. Treatment Goals and Plans

Treatment goals are objective outcomes that the patient and physician expect will result from methadone or buprenorphine maintenance treatment. Treatment plans describe the steps required to achieve the goals.

Once a goal has been defined, a brief outline of the plan for achieving that goal should be documented to help direct patient care. The following table represents examples of treatment plans and goals.

Table 1: Treatment goal and plans example

GOAL	PLAN
Stop illicit substance use Barriers are unsafe housing, drug-dealing partner and lack of non-chemical coping skills. (Recognizing some patients may never reach total abstinence from illicit opioids, documented reduction is also a reasonable goal)	• review patient weekly and adjust methadone or buprenorphine dose as necessary • refer patient to psychosocial supports such as safe housing and access to a women's shelter • monthly treatment team meeting to review progress • document reduction in illicit opioid use
Address health concerns Patient is HIV positive, has multiple skin infections and recurrent cellulitis, as well as untreated mental illness	• HIV work-up and consider referral to immunodeficiency specialist • contact street nurse re: daily change of dressings and antibiotic administration • refer to community mental health service with referral letter

3. Problematic Alcohol Use

Problematic alcohol use is the most common concurrent substance use issue in this patient population. It is critical that all patients be screened for problem drinking at initiation and intermittently. Additionally,

methadone/buprenorphine maintained patients who engage in problem drinking demonstrate poor MBMT outcomes and experience higher morbidity and mortality rates than those who do not. For this reason, patients should be advised to abstain from alcohol.

Screening, diagnosis and management protocol is available at the following link: http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/problem-drinking

4. Process (Behavioural) Addictions

Process addictions commonly occur with substance use disorders and share the common characteristics:

- cravings
- loss of control
- compulsive use
- use despite consequences

Examples of process addictions include, but are not limited to, the following areas:

- gambling
- sexual behaviours such as use of pornography, Internet or sex trade workers
- compulsive shopping, spending, or shoplifting
- eating disorders
- compulsive exercise or work behaviours

Given the connection between process addictions and substance use disorders, screening of patients for process addictions at the initial evaluation and on an intermittent basis is recommended. Evaluation for process addictions should be incorporated into a yearly review, or used in the evaluation of recurrent relapse or failure to progress through the stages of recovery.

The following clinical screening tools are useful in assessing process addictions:

1. Gambling
    - South Oaks Gambling Screen
    - Canadian Problem Gambling Index
    - Gamblers Anonymous 20 Questions

2. Sexual addiction
    - Sexual Addiction Screening Test (SAST)

MAINTENANCE AND MONITORING

1. Methadone Dosing

1.1 Initiation (Induction)

Methadone for opioid use disorder should initially be prescribed for ingestion under supervision ("daily witnessed ingestion" or "DWI") at the pharmacy. There is no clear relationship between the amount of opioid used and the dose of methadone that will be required for initiation.

The following factors will affect the amount of the initial dose required:

- amount, concentration and purity of opioid used
- accuracy of the medical and drug use history
- variation in rates of methadone metabolism
- variation in opioid cross-tolerance to methadone

Table 2: Initiation doses

Level of tolerance	Recommended daily starting dose
Non-tolerant or opioid-naive This category includes patients not currently using opioids but who are at risk of relapse.	5–10 mg/day
Unknown tolerance This category includes patients known to be using other sedative drugs or alcohol.	10–20 mg/day
Known tolerance	20–30 mg/day

During initiation, patients should be seen frequently (at least weekly) and doses should not be adjusted if patients have not been assessed face-to-face. It is important to start with a safe initial dose which does not exceed the maximum recommended starting dose of 30 mg/day.

Equianalgesic tables for converting opioid-using patients to methadone are unreliable. Such tables are **not** recommended for initiating patients onto methadone maintenance. Methadone blood levels will continue to rise for up to four to five days (half-lives) after starting or increasing a dose due to its long half-life. At day three (48 hours after the first dose), an individual's methadone blood level will be 87.5% of steady-state dose.

Most deaths occur during initiation due to too rapid dose escalation. Initiation outside of the above recommended ranges may result in patient deaths which have been associated with starting doses as low as 30 mg.

1.2 Titration

Methadone can cause fatal respiratory depression because of its long half-life and the consequent risk of drug accumulation. Patients are at high risk of overdose during the first two weeks of treatment, and while tapering at the end of treatment. The dosage must therefore be titrated carefully.

Risk factors for methadone toxicity include the following:

- other central nervous system (CNS) depressants, e.g. benzodiazepines and alcohol
- loss of tolerance, i.e. recent withdrawal, discharge from detox, jail or treatment
- medications that affect methadone metabolism
- respiratory illness
- decompensated liver disease
- advanced biological age

Note the following:

- dose increases should be no more than 10% or 5–10 mg at a time
- the interval between dose adjustments should never be less than five days (or half-lives), but may need to be longer due to the above risk factors
- patients should be seen frequently (at least weekly) during titration phase

If physicians wish to accelerate treatment, a daily clinical reassessment of the patient at three to four hours post-ingestion (peak methadone blood level) for the first three to five days after initiation or dose adjustment is required. Prescribers should not allow weekends to interrupt this process and should select a start date accordingly.

1.3 Stabilization

An effective maintenance dose:

- eliminates withdrawal symptoms for more than 24 hours
- blocks the euphoric effects of opioids
- reduces or eliminates drug craving
- does not cause excessive sedation

An adequate dose should be prescribed. For example, those who receive maintenance doses of 40 mg a day or less are five times more likely to drop out of treatment prematurely than patients who receive a dose of 60 mg or more.[16]

Many patients achieve stability on maintenance doses of 60 to 120 mg daily.

Methadone doses must always be individualized and based on clinical response.

1.4 Split Doses

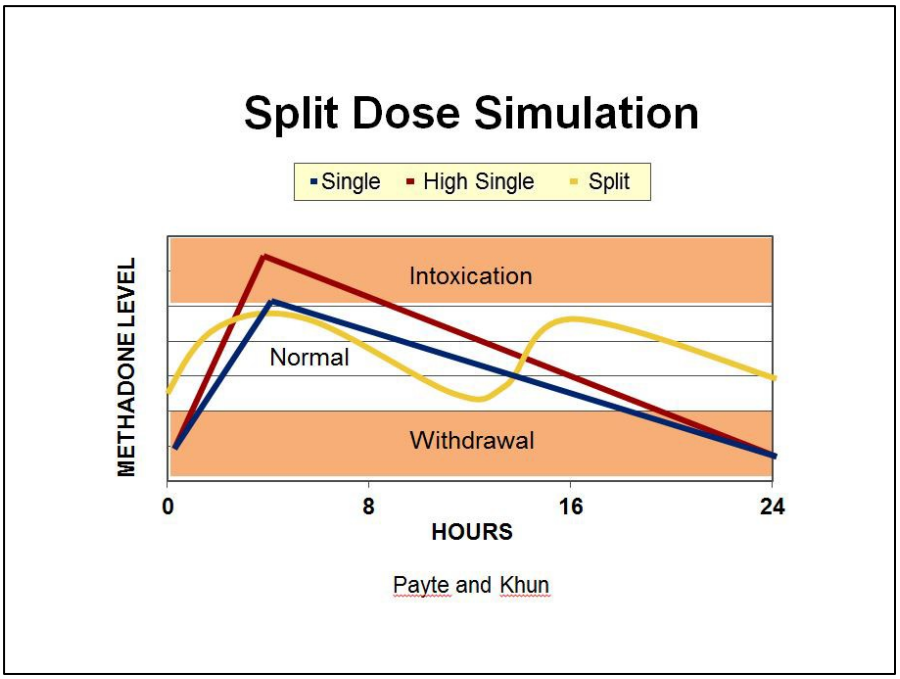
Split doses may be used in symptomatic patients who are pregnant or who demonstrate rapid metabolism. Less than 5% of patients are rapid metabolisers and this should be documented with peak and trough methadone levels. Another common cause of rapid metabolism is use of concurrent medications which induce cytochrome P450 3A4 enzymes.

- Rapid metabolizers experience symptoms of opioid withdrawal within 12 hours, even with dose escalation; methadone dose increases result in sedation with no alleviation of withdrawal symptoms.
- Split doses should not be provided in the absence of laboratory evidence of rapid metabolism because of the difficulty of ensuring twice daily witnessed ingestion and the risk of diversion of the second dose.
- Rapid metabolism is confirmed by measuring serum trough (prior to ingestion) and peak (four hours post-ingestion) methadone levels. A peak to trough ratio greater than 2:1 is consistent with rapid metabolism.
- Split dose transition: day 1 = 100% of original daily dose and 50% of the original daily dose to take in 12 hours; day 2 = 50% of original daily dose every 12 hours.

A list of medications metabolized by cytochrome P450 3A4 is available here.

16 Ball JC, Ross A. The effectiveness of methadone maintenance treatment: patients, programs, services, and outcomes. New York: Springer-Verlag; 1991.

Figure 1: Split dose simulation



1.5 Missed Doses

Tolerance is rapidly lost when methadone ingestion is interrupted or discontinued. Pharmacists are required to notify physicians of missed doses but physicians must document review of PharmaNet profiles. Physicians should let pharmacies know of their clinic policy regarding missed doses.

Suggested Protocol for Managing Missed Doses

a. One or two days missed

No change in dose is required as long as there is no other reason to withhold methadone. The reasons for the missed doses should be discussed and documented at the next visit

b. Three or four consecutive days missed

Loss of tolerance may occur in as little as three days, and the usual dose may be excessive. Recommended dosing:

- dose of 30 mg or less – continue same dose
- dose greater than 30 mg – restart at 50% of the usual dose, but the reduced dose should be no less than the initial dose of 30 mg unless there is sedative-hypnotic or alcohol use
- after tolerance to the reduced dose is demonstrated, the dose can be rapidly increased (a maximum of 10 mg per day). A slower dose escalation is suggested for patients with an unstable clinical picture or with concurrent sedative or hypnotics use. During this rapid re-titration, the patient should be reassessed at least every two days until a stable

dose has been re-established.

c. Five or more consecutive days missed
Methadone should be held until the patient has been reassessed by a physician. The remainder of the prescriptions should be cancelled. Restart at a maximum of 30 mg of methadone, then titrate with frequent re-evaluation until stable.

The reasons for the missed doses should be discussed and documented in the clinical records. The treatment plan may need to be updated.

1.6 Dosing Precautions

1.6.1 Side Effects of Methadone

In addition to profound sedation, respiratory depression and coma other side effects are:

- bradycardia and hypotension
- constipation
- perspiration
- endocrine effects/depressed libido
- xerostomia (dry mouth)
- sleep disturbance
- dysphoria
- dyspepsia
- opioid-induced edema
- pruritus
- weight gain
- cognitive impairment

Any of these side effects may occur during chronic opioid therapy but often diminish with time. Prescription medications may be required to treat these symptoms.

1.6.2 Toxicity

A list of drugs associated with QT interval prolongation is available here.

Patients at risk for methadone toxicity include those who concurrently use alcohol, sedative-hypnotics (including benzodiazepines), stimulants, illicit substances such as cocaine, or medications that interfere with methadone metabolism. An overdose can result from sudden cessation of a drug that induces methadone metabolism. There have been reports of torsades de pointes cardiac arrhythmia in patients taking high dose methadone. Metabolic disturbances such as hypokalemia are also risk factors.

It is recommended that patients who have cardiac disease, who are taking medications that prolong the QT interval or have metabolic concerns known to cause QT interval prolongation, should have an electrocardiogram (ECG) reviewed prior to starting methadone. The ECG should be repeated as clinically indicated. In patients with no other risk factors for cardiac arrhythmia, an ECG should be done if the dose of methadone exceeds 150 mg and repeated when the patients' clinical status changes.

QTc intervals greater than 450 msec should prompt review of methadone doses for other potential causes including medications which prolong QTc. Physicians should discuss the clinical implications with their patient and consider dose reduction and/or cardiology consultation.

1.6.3 Fatal Overdoses

Fatal overdoses most often occur during initiation or dose escalation or resulting from changes in prescribed medications or illicit substance use. It is essential that regular communication occurs between treating physicians, pharmacists and other health care professionals to ensure that prescribed medication changes are made safely.

Physicians must offer a prescription for naloxone for home use in case of an opioid overdose. Take-home naloxone kits are available at no cost through the BCCDC and most provincial harm reduction supply distribution (i.e. needle exchange) sites. Some patients may opt to purchase naloxone from their pharmacy without a prescription.

Fatal overdoses of methadone often occur in individuals who have acquired methadone from other individuals for whom it was prescribed. Therefore, it is important for the physician to be aware of the risk of diversion of prescribed methadone and to take responsibility for ensuring that the methadone they prescribe as **carries** is actually being taken by the patient.

Fatal overdoses are also often associated with concurrent use of:

- sedative-hypnotics such as benzodiazepines
- alcohol
- cocaine

Safety can be improved by either tapering the substance, other medications that may increase overdose risk, or by providing office- or facility-based withdrawal management (detox) prior to methadone initiation.

During the induction phase, some patients will continue to use illicit drugs. Physicians should closely monitor patients during induction and caution patients about the risk of overdose if certain illicit drugs are continued.

Prescribing physicians should be aware of factors such as the long half-life of methadone, variable rates of methadone metabolism and variation in patients' tolerance levels that can potentially lead to overdose.

2. Buprenorphine-naloxone Dosing (Reprinted from Product Monograph)

This section will be revised in the fall of 2016. In the interim, please refer to the Suboxone® product monograph and the Suboxone® Education Program: www.suboxonecme.ca.

Prior to induction with Suboxone®, consideration should be given to the type of opioid dependence (i.e. long- or short-acting opioid), the time since last opioid use, and the degree or level of opioid dependence. To avoid precipitating withdrawal, induction with Suboxone ® should be undertaken when objective and clear signs of withdrawal are evident.

- **Patients taking heroin (or other short-acting opiates):**
  For patients dependent on heroin or short-acting opioids, the first dose of Suboxone ® should be started when objective signs of withdrawal appear, but not less than 6 hours after the patient last used opioids. A score equal or greater than 13 on the Clinical Opiate Withdrawal Scale (COWS) may be a useful reference assessment.
- **Patients on methadone:**
  For patients receiving methadone, the methadone maintenance dose should be reduced to the minimum methadone daily dose that the patient can tolerate before beginning Suboxone ® therapy. The first Suboxone ® dose should be started only when objective signs of withdrawal appear (e.g. COWS score equal or greater than 13), and generally not less than 24 hours after the patient last used methadone because of the long half-life of methadone.

Baseline liver function tests and documentation of viral hepatitis status are recommended prior to commencing therapy. Regular monitoring of liver function is recommended.

2.1 Initiation (Induction) and Administration

The recommended starting dose is 4 to 8 mg Suboxone ® on day 1, initiating with 4 mg and then an additional 4 mg may be administered depending on the individual patient's requirement. The suggested total dose target for treatment on day 1 is within the range of 8 and 12 mg.

During the initiation of treatment, closer dosing supervision is recommended to ensure proper sublingual placement of the dose and to observe patient response to treatment as a guide to effective dose titration according to clinical effect.

Suboxone ® sublingual tablets should be placed under the tongue until dissolved. Dissolution usually occurs within 2 to 10 minutes.

When multiple tablets are needed to achieve optimal dosage, patient may place all tablets sublingually at the same time or in two divided portions, the second portion to be placed sublingually directly after the first portion has dissolved.

Patients should not swallow or consume food or drink until the tablet is completely dissolved.

2.2 Titration and Stabilization

Following successful induction and after the patient is receiving a stable dose, the frequency of Suboxone ® dosing may be decreased to dosing every other day at twice the individually titrated daily dose. For example, a patient who receives a stable daily dose of 8 mg may be given 16 mg on alternate days, with no medication on the intervening days. Usual maintenance doses (day 2 onward) range from 12 to 16 mg once daily (maximum 24 mg per day).

In some patients, following successful induction and after the patient is receiving a stable dose, the frequency of Suboxone ® dosing may be decreased to three times a week (for example on Monday, Wednesday and Friday). The dose on Monday and Wednesday should be twice the individually titrated daily dose, and the dose on Friday should be three times the individually titrated daily dose, with no medication on the intervening days; however, the dose given on any one day should not exceed 24 mg. Patients requiring a titrated daily dose > 8 mg/day may not find this regimen adequate.

Patients dependent upon concomitant CNS-active substances, including alcohol, should not be treated with the increased doses required by the less-than-daily dosing regimen intended for use in a supervised dose setting. Patients with sporadic use of concomitant non--opioid medications should be monitored closely, and all patients dosed on a less-than-daily basis should be observed for at least 1.5 hours following the first multi-dose administration initiating less-than-daily dosing.

2.4 Missed Doses

Missed doses are notable as they may contribute to a loss of tolerance to buprenorphine. The more doses a patient misses, the greater the loss of tolerance. Patients should be reassessed to ensure they are receiving an appropriate dose on resumption of Suboxone ® treatment. The resumption dose may need to be adjusted back to levels used during Suboxone ® induction.

If the patient has relapsed to full agonist opioids, the patient should be advised to suspend resumption of their Suboxone ® until they are in moderate opioid withdrawal due to the risk of precipitated withdrawal.

2.5 Dosing Precautions

2.5.1 Overdoses

Since buprenorphine's high binding affinity and slow dissociation make it more resistant to reversal, respiratory depression associated with buprenorphine overdose may require very high doses of naloxone such as 2 to 3 mg iv bolus and 4 mg/hour continuous infusion. Since high dose boluses of naloxone (which has a short half-life) may be displaced by buprenorphine (which has a long half-life), adequate duration of continuous infusion of naloxone is important.[17] However, even high dose naloxone (4 mg), may not reverse the effects of buprenorphine.[18] To further complicate matters, buprenorphine overdoses are usually mixed substance overdoses involving other sedatives such as alcohol, benzodiazepines.

2.5.2 Reducing Dosage and Terminating Treatment (Medical Taper)

The decision to discontinue therapy with Suboxone® should be made as part of a comprehensive treatment plan. To avoid withdrawal symptoms and potential relapse to illicit drug use, the Suboxone® dose may be progressively decreased over time in favourable cases until treatment can be discontinued. The decision to taper should be made by the prescriber, patient, and counsellor/support staff. The risk of relapse following withdrawal of treatment should be considered.

3. Urine Drug Testing (UDT)

Urine drug testing is the standard of care in methadone programs, because it provides an essential tool for the interpretation of clinical status. UDT should be provided in a respectful and a non-judgmental manner. Both supervised and random testing should be employed. UDT is helpful in:

[17] Pergolizzi J, Aloisi AM, Dahan A, Filitz J, Langford R, Likar R, Mercadante S, Morlion B, Raffa RB, Sabatowski R, Sacerdote P, Torrres LM, Weinbroum AA. Current knowledge of buprenorphine and its unique pharmacologic profile. Pain Practice 2010;10(5):428-50.
[18] Jasinski DR, Pevnick JS, Griffith JD. Human pharmacology and abuse potential of the analgesic buprenorphine. Arch Gen Psychiatry 1978;35:501-51

- evaluating compliance to methadone and to prescribed medications
- confirming self-reported use of any other substances
- detecting use of other substances which may affect safety and treatment planning
- validating abstinence outcomes

3.1 When and Why to Order UDT

- UDT must be obtained, interpreted and documented at the initial assessment as it provides information about current substance use, which aids in the diagnosis and the treatment planning process.
- The absence of opioids in the urine does not have to preclude admission to the MMP. For example, an opioid-dependent patient who is currently abstinent but at high risk of relapse, may be a good candidate for the MMP.
- UDT combined with patient self-reported substance use is more accurate than either alone.
- UDT should be performed regularly (<monthly) until the patient is stable.
- Patients on DWI methadone should be monitored with UDT as clinically indicated.

Patients receiving take-home doses should have UDTs done randomly (recommend at least four annually) as well as for cause; failure to comply with UDT should result in reassessment and return to DWI.

The BC Methadone Program provides guidelines for urine collection.

3.2 Urine Toxicology

Urine testing is able to detect use of a substance within variable time frames. Laboratory or point-of-care (POC) testing are appropriate. Physicians should make their choice after considering the advantages and disadvantages in their practice. Point of care may provide crucial information prior to writing the prescription, and is preferred by addiction specialists. Regardless of which method is chosen, physicians should ensure that both methadone and buprenorphine are included. UDT is principally based on an enzyme-linked immunoassay (EIA). On the whole, these tests are very sensitive and their detection thresholds may vary depending on the manufacturer. When interpreting results, it is important to be aware of the potential for false negative and false positive readings, as well as cross reactions. Misinterpretations can impact your patients, their treatment planning, and safety of take-home doses.

Point of care UDT for methadone maintenance can be billed to Medical Services Plan (MSP) and covers seven substances:

- amphetamines
- benzodiazepines
- cocaine metabolites

- opioids
- oxycodone
- buprenorphine
- methadone metabolites

In addition, physicians may find it helpful to test for substances prevalent in their respective communities. For example, many communities in BC have recently experienced an increase in fentanyl-related deaths, which may be consumed unknowingly by patients acquiring street opioids.

Laboratory UDT will typically detect the following substances, but it is advised to check with the local or hospital laboratory service:

- amphetamines (e.g. amphetamine, dextro and methamphetamine, MDMA (Ecstasy))
- benzodiazepines (e.g. diazepam, oxazepam, temazepam, triazolam)
- cocaine metabolite (e.g. benzoylecgonine)
- methadone metabolite (e.g. EDDP)
- opiates (e.g. heroin metabolite, morphine, codeine)

Note: Buprenorphine, oxycodone and fentanyl must be specifically requested.

Common options include:

- "confirm – if positive" via GC-MS or LC-MS
- oxycodone
- hydromorphone
- cannabinoids
- fentanyl

Caveats of UDT:

- The standard amphetamine screen does not detect methylphenidate (Ritalin) and is prone to false positive readings which a confirmation test may be necessary.
- The standard benzodiazepine screen does not reliably detect clonazepam or lorazepam and will not detect the Z drugs (zopiclone, zolpidem, zaleplon).
- The standard opiate test does not detect synthetic opioids such as oxycodone, hydrocodone, meperidine, or fentanyl—these tests must be ordered individually. Avoid the blanket term "opioids" or using trade names.
- Hydromorphone may produce a positive opiate test in high doses and it is currently not widely available as a POC test.
- Urine toxicology for alcohol is unreliable due to the rapid rate of metabolism, but ethyl glucuronide (EtG) can detect alcohol use for one to two days. (This test is outside of the MSP system.)

- Confirmatory testing (GC or LCMS) is expensive and should only be ordered if the result will alter management. It is also expensive to order uncommon substances and before doing so consider consultation with a laboratory physician.

Testing for adulterants and sample dilution is routinely performed: most laboratories will automatically test for creatinine, but only if a specimen appears clear and colourless. Creatinine levels between 0.18 and 1.8 mmol/L suggest dilution, and levels less than 0.18 mmol/L suggest substitution.
Most POC kits should have some type of adulterant screen; commonly temperature.

4. Carry Privileges

A "carry" refers to patients receiving doses of methadone/buprenorphine to be taken home for self-administration.

Patients starting MBMT must ingest methadone in the pharmacy under the supervision of a pharmacist (i.e. DWI). Patients who are biopsychosocially stable and who demonstrate appropriate UDT results may be considered for carries. The initial dose of a carry prescription is always witnessed. The decision to initiate carries can only be made by the treating physician. The reasons for granting carry privileges must be documented. Physicians must ensure that carries are safe for both patients and the public. The physician must be satisfied that safe storage of methadone will occur. Unsafe storage and diversion may result in lethal consequences.

The original 2007 manufacturer's product monograph "Serious Warnings and Precautions" section stated, "Suboxone® must be dispensed daily under the supervision of a healthcare professional, for a minimum of two months and until the patient is clinically stable and able to safely store Suboxone® take-home doses." In August 2015, the product monograph black box warning was changed to "Suboxone® must be dispensed daily under the supervision of a healthcare professional, until the patient has sufficient clinical stability and is able to safely store Suboxone® take-home doses." Although the two-month minimum has been removed, the concept of daily supervised dispensing remains, and is dependent upon the patient achieving clinical stability, which could develop sooner, or later than two months.

Although daily supervised dispensing may affect patient autonomy and convenience, safety for the patient and the community should be the priority.

4.1 Criteria for Initiating Methadone or Buprenorphine Carries

An assessment of clinical stability should be based on a combination of patient self-report, collateral information from social supports and health care providers, physical exam and interview, urine drug testing, and a review of medication adherence and PharmaNet.

4.1.1 Biopsychosocial Stability

- Patients should achieve clinical stability before receiving take-home doses of methadone or buprenorphine.
- Patients should demonstrate social, cognitive and emotional stability. This may include: the absence of suicidal ideation and psychosis, attending scheduled appointments, no missed doses, improved social relationships, stable housing, and/or returning to work or school.
- UDTs are an important measure of stability.

4.1.2 Safe Storage

- Physicians who prescribe carries are required to educate their patients on the dangers (including overdose and death) that these medications pose, especially to opioid-naive people and children. Patients must be able to store their medication safely.
- Methadone and buprenorphine should be stored in locked containers or cabinets. Carries should not be provided if safe storage cannot be ensured.

4.2 Carry Schedule

There is evidence that the effectiveness of MBMT can be enhanced by allowing carry privileges, a process known as contingency management. Progressive carry privileges should be dependent on the patient's increasing stability. Reduction or discontinuation of carry privileges should occur with evidence of instability. Criteria for assessing stability should be transparent and consistent.

Patients receiving carries must be seen at least monthly and provide unscheduled (random) UDTs.

4.3 Exceptions to Carry Guidelines

Exceptions may be granted at the discretion of the prescribing physician. Exceptions should only be initiated as a trial and be reviewed to ensure benefits outweigh risks to the patient and to the public. The reason for any exception to the carry guidelines must be documented. One example of an exception would be weekend carry doses if the patient lives in a community where the pharmacy is closed on weekends. This is in contrast to a patient who lives in a community where there are alternative pharmacies open on weekends that are reasonably accessible, but the patient prefers to go to a particular pharmacy that is closed on weekends. In the latter case, the physician should not grant an exception. Another example of an exception would be carry doses for travel. In this example, the physician could also try to arrange daily witnessed ingestion of the patient's methadone or buprenorphine at a pharmacy at the destination site where possible, particularly if the patient will be at that destination for a significant period of time.

4.4 Prescriptions for Carries

Methadone and buprenorphine prescriptions must include the total dose, the daily dose, and the first and last dates of the prescription.

If carry privileges for methadone or buprenorphine are permitted, this must be clearly documented on the prescription, including the number of witnessed ingestion doses required per week.

Carry privileges should start with one carry dose per week. With ongoing demonstration of stability, the number of carry doses per week can be increased in a stepwise fashion. Most stable patients are established on twice weekly witnessed ingestion. This is a reasonable balance between safety and patient inconvenience. Some long-term stable patients may be considered for once-weekly witnessed ingestion. Physicians should document the need for carries and their benefits, and exceptions to guidelines.

When there are multiple DWI days, they should be staggered, not consecutive. For example, “witness two days a week” should be on Monday and Thursday rather than Monday and Tuesday, with carries the rest of the week. “Witness three days a week” should be on Monday, Wednesday and Friday, not three consecutive days then four days of carries. Noting specific days of the week is preferable to the number of doses.

4.5 Reassessment of Carry Privileges

Patients who demonstrate instability must be reassessed. Signs of instability include:

- clinical evidence of non-prescribed psychoactive substance use
- missed appointments with physicians, or other supports
- missed methadone or buprenorphine doses
- repeated requests for early release or extension of carries
- requests for increasing a previously stable methadone or buprenorphine dose
- reports of lost, spilled, stolen or vomited methadone or buprenorphine positive UDT
- non-attendance for random UDT

Physicians are responsible to their patient and the public to take appropriate steps to minimize the possibility of diversion of all prescription opioids including methadone and buprenorphine.

The patient’s clinical stability should be reassessed periodically and documented. If the patient’s status becomes unstable, then carry privileges should be suspended, and reinstituted in a step-wise manner after stability is reestablished. Note that if an unstable patient has been diverting, or not taking their full dose, tolerance may be lost and reinstitution of DWI may require dose reduction and close monitoring.

5. Multi-modal Psychosocial Spiritual Approach

Many methadone or buprenorphine patients struggle with a number of challenges, such as poverty, lack of education, employment and housing, exposure to violence, poor nutrition, serious physical or mental health problems and involvement with the criminal justice system. These problems are not addressed with the provision of medication alone. The role of the physician is to identify strengths and needs in order to develop and address an individual care plan. Use of a strength-based model or a solution-focused practices approach can provide positive support to the patient. Programs that do little more than provide a methadone or buprenorphine prescription are inadequate; programs are expected to incorporate a comprehensive biopsychosocial and spiritual approach to treatment. Complex patients are best managed in a setting where intensive case management is available.

5.1 Transtheoretical Model of Change

The process of change has been conceptualized by J.O. Prochaska and C.C. DiClemente as a series of stages through which individuals may move cyclically until permanent change has occurred. These stages are as follows:

- pre-contemplation
- contemplation
- preparation
- action
- maintenance
- relapse

Motivational interventions must match the patient's stage of change. Patients will quickly become frustrated when the intervention offered is out of step with their own view of the problem. For example, if a patient has only just started to weigh the pros and cons of whether or not a particular issue is a problem (the contemplation stage), recommending a particular solution (action stage) will only elicit resistance and be counterproductive.

The table titled Appropriate Motivational Strategies for Each Stage of Change suggests several interventions for each stage of change.

5.2 The Prescriber's Role

Treatment goals are best achieved in the context of trusting, therapeutic relationships with patients, to promote maximal benefit and reduce risk of loss of retention to care. Physicians should offer non-judgmental, collaborative environments in which patients feel safe to discuss their concerns.

Once constructive relationships have been established, physicians must work with patients to identify aspects of each patient's life that could be changed or modified to benefit the patient. These treatment

goals should be identified collaboratively between the patient and the physician. Many appropriate treatment goals are not necessarily focused on drug-using behaviour. For example, patients may wish to move to better or safer housing, improve their general health, seek treatment for mental health issues, enroll in training programs, learn better communication skills, learn relaxation techniques or improve the quality of their personal relationships.

After goals have been identified, methadone/buprenorphine prescribers should work with patients to develop treatment plans to meet these goals. This progress should be monitored and outcomes documented. Achieving these goals may involve referral to community resources or specialized services.

5.3 Brief Interventions

Substance-dependent patients are often described as lacking motivation to change, especially if that change requires some self-organization. Prescribers can effectively use frequent brief interventions to encourage patients lacking self-motivation.

Examples of opportunities for brief interventions include:

1. Building a therapeutic relationship
    - Demonstrate sustained interest and concern for patients' progress.
    - Schedule regular visits and ensure that two-way communication exists.
2. Education
    - Provide factual drug information and information on post-acute withdrawal syndrome.
    - Educate patients regarding the symptoms of impending relapse, such as exhaustion, complacency, impatience, dishonesty, self-pity, frustration, and depression.
    - Discuss behaviours such as denying, minimizing, rationalizing, intellectualizing and compartmentalizing.
3. Goal planning
    - Consider all areas of patients' lives, not just substance use issues.
    - Prepare and document plans on how to avoid drug using situations.
    - Identify and help remove impediments to change, such as the need for childcare or transportation.
    - Remind patients that it is better to reach a modest goal than to aim for, but fail to reach, a more ambitious target. Coach patients to take small steps on the road to recovery.
    - Revisit goals regularly, and modify accordingly.
4. Promoting self-awareness and positive behaviours
    - Identify internal and external triggers for relapse.
    - Avoid dwelling on failures. Help patients take pride in and build on their successes.
    - Encourage harm-reduction behaviour (e.g. accessing harm reduction supplies and/or services, take-home naloxone)
    - Encourage patient to exhibit self-compassion

5.4 Biopsychosocial Support

Patients with substance use disorders may struggle with multiple psychological and social problems, and combining methadone or buprenorphine with specific biopsychosocial interventions has been shown to lead to improved treatment outcomes.[11] These interventions can range from regular follow-up with psychosocial support from the prescriber, to programs available in the community, to specific psychological therapies such as motivational interviewing, CBT or case management. Patients may live in areas where these interventions are unavailable, or may resist referral to counsellors, but this should not prevent physicians from counselling patients, and should never preclude patients being offered treatment with methadone or buprenorphine.

Depending on a patient's circumstances, physicians may opt to work in collaboration with counsellors, or may refer patients to independent counselling agencies or self-help groups such as Alcoholics Anonymous (AA) or Narcotics Anonymous (NA) and Self-Management and Recovery Training (SMART). Many other specialized resources may be available to aid MBMT patients. Physicians are expected to familiarize themselves with the full spectrum of services available to their patient population through their local health authorities, and are encouraged to refer their MBMT patients to appropriate community treatment programs, support groups and counsellors.

All publicly funded treatment facilities located throughout British Columbia fall under the jurisdiction of the health authorities. The range of options for treatment of substance dependence includes outpatient counselling services, withdrawal management, intensive residential treatment, support recovery and other forms of supportive housing. Many of these ancillary treatment options are available to patients on methadone or buprenorphine. Methadone/buprenorphine prescribers and clinics are advised to take advantage of the resources available to their patients and to refer appropriate MBMT patients to community treatment facilities, support groups (including 12-step) and counsellors for additional support. Patients should also be advised of other community resources which may include, but are not limited to, peer support groups (such as Narcotics Anonymous, Alcoholics Anonymous or Rational Recovery) or support offered through the patient's religious or spiritual connections.

Physicians should document the issues each patient is attempting to address, resources offered, and what progress has been made. Refusal or unavailability of psychosocial support should never preclude patients being offered treatment with methadone or buprenorphine.

6. Documentation of Benefits

An assessment of the patient's perspective of treatment benefits is important to evaluate and compare to objective measures. Not every opioid-dependent patient will benefit from MBMT. Like any other medical treatment, there are risks and benefits associated with this treatment.

Methadone/buprenorphine prescribers must clearly document the benefits derived from MBMT in each patient's chart, and also develop and record a treatment plan outlining how further benefits (goals) are to be achieved. Documenting the benefits of MBMT is the standard of care. In addition to recording the dose of methadone or buprenorphine prescribed at each visit, reference to parameters of benefit and current treatment plans should be recorded.

6.1 Categories of Benefits

The benefits of methadone/buprenorphine maintenance treatment fall into seven categories. Methadone/buprenorphine prescribers may find the following list useful for assessing their patients' progress, and for formulating and monitoring treatment plans:

1. reduction or cessation of opioids use, particularly injection
2. reduction or cessation of other psychoactive substance use
3. improved mental and physical health
    - improved mental health outcomes
    - decreased incidence of concomitant infections such as endocarditis, osteomyelitis, and cellulitis, with consequently reduced need for hospitalization
    - decreased emergency room visits for drug-related complications
    - improved hepatitis C (HCV) and HIV clinical parameters
    - improved engagement with primary care
    - improved nutrition and weight gain
    - improved pregnancy outcomes
4. decreased involvement with the criminal justice system
5. improved living situations – severe OUD often results in homelessness or unsafe living conditions; methadone/buprenorphine maintenance patients should be encouraged to seek drug- free accommodation, as this is optimal for successful recovery; improved living situations might include an environment with sober friends, or safe long-term, drug-free housing as well as other forms of supportive housing
6. Improved social and personal relationships
7. Improved vocational and employment opportunities
8. Patients who attain improved medical and social stability are much more likely to connect with social agencies to gain access to financial support; they are also more likely to be considered for educational and training programs which may be necessary for eventual employment

7. Prescriptions for Methadone and Buprenorphine Maintenance

Safe methadone prescribing depends on good communication between patients, physicians, pharmacists and other health care providers.

1. Methadone maintenance prescriptions must be written only on designated methadone maintenance controlled prescription forms (see figure 2). **Note that these prescriptions will be considered void if the preprinted text is altered. It is permissible to mark an "x" in the home delivery box if you do not want to authorize home delivery.**

Figure 2: Methadone maintenance controlled prescription form

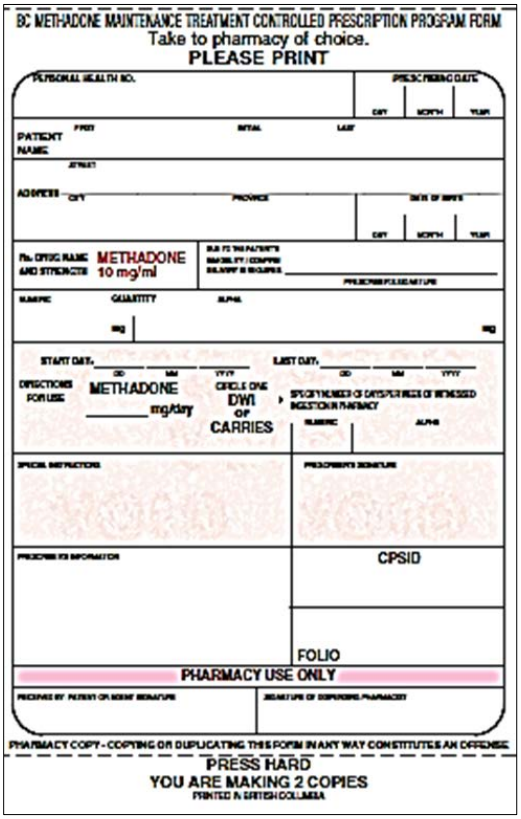
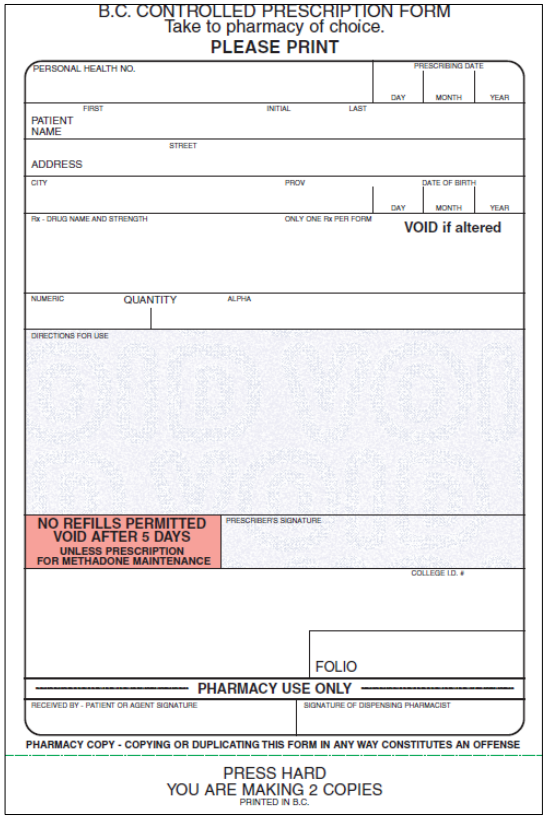


Figure 3: Duplicate controlled prescription form



2. The methadone maintenance controlled prescription form is to be used for prescribing Methadose® for OUD, and must specify the following:
    a. daily dosage in mg, with inclusive start and stop dates
    b. if the patient is restricted to daily witnessed ingestion (DWI) in pharmacy or if carry privileges are allowed

i. if carry privileges are allowed, physicians must specify the number of witnessed ingestions
ii. if specific dates are not indicated by the physician on the methadone maintenance controlled prescription form, the days for witnessed ingestion are set to maximize the number of days between witnessed ingestions by the College of Pharmacists of British Columbia
iii. the total quantity prescribed must exactly match the dispense dates (no rounding up)

3. The regular duplicate controlled prescription form is to be used for all prescriptions for methadone for analgesia, as well as prescriptions for formulations of methadone other than Methadose® (e.g. Metadol® tablets), even when prescribed for OUD. **Buprenorphine prescriptions are to be written on the duplicate prescription, but with the addition of start/stop dates and DWI/carries, similar to methadone for OUD prescriptions.**

4. If any change occurs prior to the completion of a current prescription, a new prescription must be issued and include instructions to cancel the previously issued prescription. Pharmacists do not have independent authority to make any alterations or changes to a Methadone Maintenance Controlled Prescription form. Any required or requested change(s) must be patient-specific and authorized by the patient's prescriber through direct consultation with the pharmacist. Any prescriber-authorized changes must be confirmed in writing, signed by the prescriber, received by the pharmacy (fax is acceptable) prior to dispensing the medication whenever possible and attached and filed with the original prescription.[19]
5. Physicians' copies of the controlled prescription forms must be retained with the patient record and must be identical to the copies issued to the patients.
6. Prescriptions for methadone may only be faxed under extenuating circumstances and to the physician should directly communicate with the pharmacist. In these exceptional cases, the original prescription must be sent to the pharmacy by the next business day.
7. The use of previously signed blank prescription forms is unacceptable.
8. In order to provide continuity of care to patients who are receiving treatment in hospitals or health authority programs who do not have an on-site pharmacy to dispense and witness methadone, it is suggested that:
    a. the physician write the prescription of no more than seven days supply to be dispensed by a community pharmacy as a "carry" and it to be "delivered"
    b. marking the name of the regulated *(HPA)* health care professional responsible for receiving, securely storing and administering the methadone delegated by the patient
    c. marking the name of the hospital or health authority program regulated in the province of British Columbia
    d. returning the methadone to the pharmacy if not administered

[19] College of Pharmacists of British Columbia Professional Practice Policy #66: Policy Guide: Methadone Maintenance Treatment (2013); Principle 2.2, page 6.

DISCONTINUATION OF METHADONE OR BUPRENORPHINE MAINTENANCE TREATMENT

There is medical evidence that patients who remain in long-term MBMT continue to derive benefit. Success of treatment is directly proportional to the length of time on treatment. There is also evidence that the majority of patients who discontinue MBMT prematurely are at risk of relapse to non-medical opioid use within one year.

Methadone/buprenorphine maintenance treatment may be discontinued when:

- treatment goals have been achieved and patient wishes to discontinue MBMT
- treatment goals not achieved but patient wishes to discontinue MBMT despite medical advice
- involuntary dismissal from MBMT

When buprenorphine is discontinued, peak intensity of withdrawal symptoms occurs three to five days later, and lasts eight to 10 days. Compared to methadone, buprenorphine withdrawal tends to be associated with a lower intensity of withdrawal symptoms.[20] Abrupt cessation of either medication can lead to severe withdrawal symptoms which cause emotional and physical distress and can in turn lead to relapse or unintentional overdose. At the start and end of treatment, patients are particularly vulnerable; ensure the patient understands the risks and document discussion of take-home naloxone doses.

1. Discontinuation in Stable Patients: Treatment Goals Achieved

Optimum benefits from MBMT are not realized for at least a year. Generally, patients who have been on the MBMT for two or three years will have better outcomes when tapered off methadone or buprenorphine, compared with those who start the tapering process before two years of treatment.

In order to reduce the risk of relapse, patients should be encouraged to stay in MBMT, although the decision whether or not to discontinue ultimately lies with the patient. The following goals are associated with a reduced risk of relapse while engaged in MBMT and following discontinuation:

- long-term abstinence from opioids and other psychoactive drugs
- development of non-chemical coping skills

[20] Fudala PJ, Jaffe JH, Dax EM, Johnson RE. Use of buprenorphine in the treatment of opioid addiction. II. Physiologic and behavioural effects of daily and alternate-day administration and abrupt withdrawal. Clin Pharmacol Ther 1990;47:525-534.

- stable housing
- stable mental and physical health
- development of supportive relationships with people without substance use disorders
- stable source of income
- slow gradual reduction of methadone/buprenorphine, during which patients are monitored for signs of instability or relapse

Patients who continue to benefit from methadone/buprenorphine and do not wish to be tapered should not be pressured to do so.

Literature suggests that the maximum weekly reduction of methadone should be no more than 5% of the total dose in order to minimize withdrawal symptoms and the risk of relapse. In the case of buprenorphine, patients can do well reducing by 2-4 mg if the dose range is 8-24 mg. The taper should be slowed considerably when the patient reaches 4-6 mg/day. The last 2 mg of buprenorphine takes the longest to reduce and may require cutting tablets in order to taper gradually. Even going from 2 mg to 1 mg is difficult for most patients.

Patients frequently request more rapid tapering, and it is important that physicians explain the dangers of rapid tapering. Tapering should be undertaken as a trial. Patients who feel at risk or relapse to opioids or decompensate in other aspects of their lives during or after tapering should be offered re-entry to MBMT and re- stabilized. Patients should not be penalized for unsuccessful tapering from MBMT.

2. Discontinuation in Unstable Patients: Treatment Goals Not Achieved

Some patients choose to taper MBMT despite its benefits even though they are not yet fully stable. In this case, tapering will place patients at high risk for relapse. The physician and health care team should explore the patient's motivation for tapering and provide alternative treatment options. Physicians may recommend continuation in MBMT, but if patients still insist on withdrawing from methadone or buprenorphine, the patient and physician should collaborate with the pharmacist and prepare a plan for a trial of tapering, taking into consideration the relevant risks. Overdose prevention counselling, harm reduction education and a take-home naloxone kit are strongly recommended for patients who are unstable and discontinuing treatment. Patients who relapse to non-medical opioids, become unstable, or alter their decision to taper at any time should be encouraged to re-engage MBMT and return to a stabilizing dose.

3. Involuntary Dismissal

Patients not demonstrating objective benefits from MBMT should have their treatment plans re-evaluated and be offered all reasonable interventions, including transfer to another methadone or

buprenorphine treatment provider. Should they still continue to fail to demonstrate objective benefits and all interventions have failed, they should be tapered from MBMT and offered alternative treatment, including referral to harm reduction services and take-home naloxone. Discontinuation of methadone or buprenorphine should not result in disruption of patients' use of available primary care or mental health services. Dismissal does not mean that patients should not be considered for readmission to the program at a later time.

Patients who are in violation of significant sections of their agreements should be tapered off methadone or buprenorphine at a reasonable schedule; however, if patients are verbally abusive or threaten clinic staff with violence, this schedule can be accelerated at the discretion of the prescriber. If a physician feels unsafe while treating a patient, the physician may provide the patient with a two-week DWI tapering prescription, instructions on obtaining take-home naloxone, and discontinue the physician-patient relationship.

4. Transfer of Care

The patient or the physician may decide that the responsibility for prescribing methadone or buprenorphine should be transferred to another prescriber.

The physician assuming care of the patient is responsible for contacting the previous MBMT prescriber in order to obtain appropriate clinical information and verify treatment medication dosage, concurrent medications (including non-prescription whenever possible) and transfer date. Mutual agreement regarding the transfer date (and detailed documentation) is critically important to ensure that a double dose is not given. It is not sufficient to communicate with the previous prescriber merely by leaving messages or contacting the physician after MBMT has begun.

Patients who have recently been released from correctional facilities will have been transferred to the correctional facility physician and need to be transferred back to their previous community prescriber(s). If there is a new prescriber, the new prescriber should communicate with the previous prescriber, to facilitate continuity of care. See Special Populations for more information.

Documented review of the PharmaNet profile can also provide information on previous methadone or buprenorphine prescribers.

In all cases, the new prescriber must perform an updated comprehensive biopsychosocial assessment and physical examination with appropriate laboratory investigations and create a treatment plan that takes into account all the previous MBMT physician's treatment concerns. If, for example, collateral information about a patient's inappropriate or threatening behaviour as the reason for transfer is not conveyed by the previous physician or included in the new prescriber's treatment plan, it is likely that the new prescriber will be subjected to the same behaviour pattern.

In addition, patients may transfer from one prescriber to another, because of previous involuntary discharge due to diversion or inappropriate use of carries. This information is essential for the new prescriber in order to alter the treatment plan for that patient

ADVICE TO PHYSICIANS DOWNSIZING OR LEAVING THEIR METHADONE OR BUPRENORPHINE MAINTENANCE PRACTICES

- When planning to discharge or transfer a methadone/buprenorphine maintenance patient due to downsizing or leaving your methadone/buprenorphine maintenance practice, physicians should remember that patient safety is the primary concern.
- Appropriate communication with other treating physicians and pharmacists is essential for the safe continuity of care of methadone/buprenorphine maintenance patients.
- When considering tapering or transferring a patient, physicians should remember that this should only be done for reasons of clinical appropriateness.
- If it is necessary to provide bridging prescriptions during patient transfer to another prescribing physician, these prescriptions should be clinically appropriate and should not compromise patient or public safety.
- If it is not possible to transfer a patient to another treating physician, then medical office staff should provide patients with written information about alternative local resources (a list of methadone clinics accepting new patients is available on the College website).
- Any physician who is leaving practice should be aware that the College has a guideline titled *Leaving Practice*, and it is the College's recommendation that three months' notice is a reasonable time to allow a patient to find a new treating physician.

SPECIAL POPULATIONS

1. Introduction

All patients require a comprehensive initial assessment.

This section will deal with the following populations:

- adolescent patients
- women of child-bearing potential
- pregnant women
- non-injecting opioid-dependent patients
- patients with comorbid conditions
- hospitalized patients
- provincial and federal corrections patients
- patients who wish to travel

2. Adolescent Patients

Adolescents with mild opioid use disorders, with intact support systems, may be considered for programs involving intensive in-patient or outpatient psychotherapy. Pharmacotherapy may or not be part of treatment.

Adolescent patients who meet the criteria for moderate to severe opioid use disorders may benefit from medication-assisted treatment. Currently in Canada, buprenorphine-naloxone is indicated for patients 18 years of age or older. Prescribing buprenorphine-naloxone to patients under 18 would be off-label, and consent should be obtained from the patient or guardian, after discussion of the risks and benefits. A frequently reviewed treatment plan, under the guidance of a practitioner experienced with working with substance-dependent youth, is advised.

As with all patients, adolescent patients should be maintained on MBMT only if the benefits of treatment can be clearly documented.

3. Women of Child-bearing Potential

Women seeking treatment for opioid use disorder may have a number of predisposing psychosocial risk factors for drug use and have experienced multiple adverse consequences. Their histories may include disrupted family lives, physical violence, incarceration, sexual assault, sex trade work, child custody issues, unstable housing, mental health issues (such as mood and personality disorders), and physical

health issues (such as HIV, hepatitis C virus or STIs). Physicians should be aware that the different causes of addiction, patterns of use and reasons for relapse are often gender-specific. Clinicians can offer more effective treatment by being conversant in the identification and treatment of these issues as they apply to women.

Knowledge of other community resources (for example, PEERS, a rehabilitation program for sex trade workers, based in Vancouver and Victoria) is also essential in treating women with opioid dependence. Many other resources in BC can be found on Red Book Online, an online directory of services for the lower mainland. Treating opioid-dependent women with respect and compassion is fundamental to their recovery.

Opioid dependent women commonly experience menstrual irregularity and amenorrhea. For many women, this will be regulated and ovulation will start once they are stabilized on methadone. All women of child-bearing age should have a pregnancy test at the initial triage visit and periodically thereafter.

Birth control should be offered to all women upon initiation of methadone or buprenorphine. When stable non-pregnant women suddenly feel the need to increase their methadone or buprenorphine dose, consider the possibility of pregnancy. Depo-Provera® and progesterone-impregnated intrauterine devices (IUDs) are the least expensive and the most reliable option in this often unstable population. Oral contraceptives can be taken daily with methadone to reduce missed doses. Pharmacists will sometimes allow patients to store their OCPs at the pharmacy. The availability of free condoms in the office will also encourage women patients to practise safe sex (these are obtainable from health authorities and public health departments).

Women maintained on methadone or buprenorphine should be encouraged to remain on MBMT, as maternal withdrawal can lead to poor pregnancy outcomes such as low birth weight, poor fetal neurological development and a risk of placental abruption.

4. Pregnant Women

Buprenorphine-naloxone is contraindicated in pregnancy; however, physicians may contact Health Canada's Special Access Programme to obtain authorization for the buprenorphine-only product. In this section, the term buprenorphine applies to the buprenorphine-only product.

4.1 Introduction

The quality and nature of the initial encounter is crucial when providing prenatal care for pregnant women who use opioids. By providing non-judgmental care, physicians support these women's self-

determination and increase the chances of engaging in treatment.[21] The most effective care for pregnant women with substance use problems involves a collaborative approach by physicians, midwives, nurses and social workers, in hospital and the community.[22]

Opioid use is a powerful self-medication for blocking intrusive thoughts, avoiding feelings and achieving sleep. Many women who use substances have a history of physical, sexual or emotional trauma.[23] Physicians should be aware of and address issues of power (for example, loss of carries) with this knowledge in mind. Women may present late in pregnancy due to additional barriers such as fear of losing their children. Some women may be uncertain of dates due to their chaotic lifestyle or menstrual irregularities.

MMT is the treatment of choice throughout pregnancy and the postpartum period for opioid-dependent women.[24, 25] Women who are engaged in MMT experience better pregnancy and birth outcomes than those who continue to use non-medical opioids. Pregnancy complications due to illicit opioid use include intrauterine growth restriction (IUGR), low birth weight and premature labour (due to opioid withdrawal), and risk of hepatitis C and HIV with needle use.[26, 27] Methadone has been shown to be beneficial in the reduction of maternal relapse, particularly when a comprehensive system of support is in place.[28]

4.2 Guiding Principles in Pregnancy

1. **Respect is key:** Guilt and shame about substance use, fear of being judged and of having children removed are major barriers to care. A respectful approach acknowledges that change is a process and meets women at their stages of change.[29, 30]
2. **Informed choice:** All women who are pregnant and using substances are informed by their health-care providers of their choices and rights at all steps of the care process. Side effects of methadone/buprenorphine treatment are described and discussed. If a woman elects not to pursue medication-assisted treatment, the risks and benefits should be carefully explained and documented. Tapering off methadone or buprenorphine during pregnancy, while still the

[21] Motz M, Leslie M, Pepler D, Moore JTE, Freeman PA. Breaking the cycle: measures of progress 1995–2005. JFAS int. 2006; Suppl 4;e22.
[22] National Treatment Agency for Substance Misuse. Engaging and retaining clients in drug treatment. London: National Health Service; 2004.
[23] Haskell L. First stage trauma treatment: a guide for mental health professionals working with women. Toronto: Centre for Addiction and Mental Health; 2003.
[24] Jones HE, Martin PR, Heil SH, Kaltenbach K, Selby P, Coyle MG, et al. Treatment of opioid-dependent pregnant women: clinical and research issues. J Subst Abuse Treat; 2008 Oct; 35(3)245–59.
[25] Winklbaur B, Jung E, Fischer G. Opioid dependence and pregnancy. Curr Opin Psychiatry. 2008;21(3):255–9.
[26] Centre for Addiction and Mental Health. Exposure to psychotropic medications and other substances during pregnancy and lactation: a handbook for health care providers. Toronto: Centre for Addiction and Mental Health and Motherisk; 2008.
[27] The PRIMA (Pregnancy-Related Issues in the Management of Addictions) Project [Internet]. Ordean A, Midmer D, Graves L, Payne S, Hunt G, the PRIMA Group. Toronto: Department of Family and Community Medicine, University of Toronto; 2008. Opiates [updated June 2008; cited 2009 Mar 5]. Available from: http://www.addictionpregnancy.ca/opiates.html.
[28] Jones HE, Martin PR, Heil SH, Kaltenbach K, Selby P, Coyle MG, et al. Treatment of opioid-dependent pregnant women: clinical and research issues. J Subst Abuse Treat; 2008 Oct; 35(3)245–59.
[29] Rollnick S, Miller WR, Butler CC. Motivational interviewing in health care. New York: Guilford Press; 2008.
[30] Prochaska JO, Norcross J, DiClemente C. Changing for good. New York: Avon Books; 1994

patient's choice, is not medically advised.

3. **Working from strengths:** Strengths and protective factors of each woman, her family and community are recognized and enhanced.[31]

4. **Reducing harms:** Helping women reduce the harms associated with substance use, such as facilitating access to general medical care, addressing homelessness, and providing other supports will improve outcomes for women and children.

5. **Addressing violence:** Understanding the impact of violence against women, including the high incidence of post-traumatic stress disorder (PTSD).

6. **Culturally sensitive care:** Understanding cultural, racial and religious differences in the provision of methadone care.

7. **Respecting all goals for change** in substance use along the continuum from reducing use to abstinence, using early intervention strategies, medical and psychological treatment and follow-up supports.

8. **Teamwork:** All care team members, including the patient, share the decision making, development, implementation and monitoring of a single service plan.

9. **Preserving the mother-infant bond:** Supporting measures such as hospital rooming-in and breastfeeding.

Pregnancy provides a "window of opportunity" to motivate substance-using women to make changes in their lives.

4.3 Management

Acute withdrawal in pregnancy increases the risk of preterm labour or miscarriage. Rapid uptake into treatment, active ongoing support and practical measures to encourage attendance are all approaches that research suggests improves engagement[32] and continued access to care. Methadone initiation is most efficient in an in-patient setting; however, outpatient initiation is practical and appropriate when in-patient treatment is not an option.

[31] Weaver SM. Shame reduction: a model for training child welfare workers on best practices with mothers who use substances. In: Poole N, Greaves L, editors. Highs and lows: Canadian perspectives on women and substance use. Toronto: Centre for Addiction and Mental Health; 2007, p. 283–8.
[32] National Treatment Agency for Substance Misuse. Engaging and retaining clients in drug treatment. London: National Health Service; 2004.

4.3.1 Initial Assessment

In addition to the routine assessment, assessment of pregnant patients should include:

- Complete medical history, including substance use history, obstetric history and assessment of the patient's risk factors for exposure to infectious diseases
- Assessment for mental health comorbidities
- Assessment of personal safety, nutritional and housing needs
- Complete physical and fetal examination, including measurement of fetal heart rate for baseline (if the patient is more than 14 weeks pregnant)
- Completed Part 1 of the BCPHP British Columbia Antenatal Record
- Appropriate laboratory testing, including prenatal blood work, hepatitis C serology and liver function tests
- Ultrasound to estimate gestational age of the fetus
- UDT to confirm opioid use, and to provide information about other drug use which is essential in the treatment planning process—an opioid negative UDT does not preclude admission if the assessment confirms that MMT is appropriate
- a treatment plan for other substances used, including alcohol

4.3.2 Prenatal Management

- An effective dose of methadone is one that prevents withdrawal symptoms and reduces cravings for 24 hours.
- An adequate methadone dose will protect the fetus from repeated withdrawal.
- Recent studies have shown that higher doses of methadone do not correlate with the occurrence or severity of neonatal abstinence syndrome (NAS).[33]
- Higher doses of methadone are often needed as pregnancy advances due to increased blood volume, especially in the third trimester.[34]
- Split methadone doses may be needed to deal with increased hepatic metabolism and to prevent day-to-day withdrawal symptoms.[35]
- Carry doses should only be provided to stable patients. Indicators of stability include negative random UDTs, safe and supportive drug-free housing, safe methadone storage facilities, and appropriate relapse prevention plans.

4.3.3 Third Trimester

- The planning around hospital admissions for birth should be coordinated as early as possible between the maternity care teams, the methadone prescriber and the patient.

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[33] Berghella V, Lim PJ, Hill MK, Cherpes J, Chennat J, Kaltenbach K. Maternal methadone dose and neonatal withdrawal. Am J Obstet Gynecol. 2003;189(2):312–7.
[34] New South Wales Department of Health. National clinical guidelines for the management of drug use during pregnancy, birth and the early development years of the newborn. North Sydney (Australia): NSW Department of Health; 2006
[35] Jones HE, Martin PR, Heil SH, Kaltenbach K, Selby P, Coyle MG, et al. Treatment of opioid-dependent pregnant women: clinical and research issues. J Subst Abuse Treat; 2008 Oct; 35(3)245–59

- If a dosage increase is needed, it can be done in steps of 5 mg to 10 mg per week as an outpatient. Physicians can consider split doses in pregnant women who experience early withdrawal due to changes in methadone metabolism, to keep the total amount of the dose down and to even out blood levels over a 24-hour period. For example, two-thirds of the dose can be taken as DWI in the morning, with the remaining one-third dispensed as carries for the evening. Note that split dosing can increase the risk of diversion.

4.3.4 Intrapartum

- Methadone is not used as pain control. Regular methadone dosage should be continued and not considered as part of the pain management plan.
- Regular labour and delivery pain medication can be used. Epidural anesthesia is the preferred analgesic method due to altered pain perception in this population. Nitrous oxide may be useful in the second stage. Opioid analgesics may be used but the dose may need to be increased due to tolerance and the patient must be monitored for somnolence and respiratory depression.
- When methadone-maintained women present in labour, methadone can be given in a decreased volume of fluid (by arrangement with the pharmacy).
- If oral fluids are contraindicated, methadone should be replaced with parenteral opioids.
- Mixed agonist/antagonists are contraindicated as they will precipitate acute withdrawal.
- Sensitivity is needed during intrapartum and postpartum pain management. Many women who use substances have experienced sexual trauma and PTSD. Vaginal exams or the pain of childbirth can trigger symptoms which in turn may cause intensification of labour pain.

4.3.5 Postpartum

- Postpartum maternal methadone requirements usually drop due to a decrease in blood volume and changes in metabolism. Consequently, the dose may need to be decreased over a few days or weeks. A split dose will generally no longer be required.
- Daily witnessed ingestion of methadone for unstable patients is recommended. It may be difficult for new mothers to go to the pharmacy daily, therefore the risks versus the benefits of granting carry privileges must be carefully considered.
- Continuation of methadone is a joint decision between the patient and her physician. Stability is the goal, and if patients choose to withdraw from methadone, they should be informed of the risk of relapse and offered relapse prevention strategies.

4.3.6 Breastfeeding and Methadone or Buprenorphine

- Breastfeeding is compatible with MMT, and is encouraged, regardless of the maternal dose.[36, 37] (**Note:** Due to limited human data, patients should be advised of the risks versus the benefits of breastfeeding while taking buprenorphine. This section will be updated in the fall of 2016.)
- Breastfeeding is contraindicated in active substance-using and HIV-positive patients.
- Studies to date evaluating the effect of breastfeeding on HCV transmission indicate that breastfeeding does not appreciably increase the risk of transmitting HCV to a neonate.

4.3.7 Urine Drug Testing (UDT)

- UDT is always collected at the initial visit to confirm opioid use. Results also provide information about other drug use. This information is essential in the treatment planning process.
- Pregnant patients should provide UDTs at the same frequency as other MBMT patients depending on stability, including random sampling.
- A positive UDT or self-reported drug use is not an indication for an involuntary taper or withdrawal from methadone and should never preclude medical care. Even with continued use of illicit drugs, continued contact with health-care providers improves pregnancy outcomes and builds trust. Unstable patients must remain on daily witnessed ingestion.
- Carries are a privilege and should only be granted to stable patients (e.g. negative UDTs, safe housing, and relapse prevention plans in place). Carry privileges are not recommended for pregnant women who do not provide random UDT.

4.3.8 Prenatal Methadone Withdrawal Management

- The standard of care for pregnant opioid-dependent women is MMT throughout pregnancy and postpartum. However, some patients insist on detoxification from all drugs during pregnancy. Patients insisting on withdrawal or tapering should be informed that the risk of relapse with dose reduction or discontinuation of methadone in pregnancy is high and no less than in other patients.
- The patients who are most likely to be successful in withdrawal during pregnancy and to remain drug free are those who have had prolonged stability on methadone, have had drug treatment including relapse prevention and are socially stable.

4.3.9 Neonatal Abstinence Syndrome (NAS)

- Some infants exposed to opioids during pregnancy undergo withdrawal. If withdrawal occurs, the onset of symptoms depends on the half-life of the substance used and when the last dose was taken.
- The occurrence and severity of NAS does not correlate with higher maternal methadone dose.

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[36] Jansson LM, Choo R, Velez ML, Harrow C, Schroeder JR, Shakleya DM, Huestis MA. Methadone maintenance and breastfeeding in the neonatal period. Pediatrics. 2008;121(1):106–14.
[37] Wilbourne P, Wallerstedt C, Dorato V, Curet LB. Clinical management of methadone dependence during pregnancy. J Perinat Neonatal Nurs. 2001;14(4):26–45.

- NAS is always a diagnosis of exclusion. When NAS is suspected, other diagnoses such as hypoglycemia, hypocalcemia and sepsis should be ruled out first.
- Infants of mothers who used prescription drugs during pregnancy, especially benzodiazepines, barbiturates and antipsychotics, as well as alcohol and nicotine, may have neonatal withdrawal symptoms for a longer duration.
- Rooming-in with the infant, frequent skin-to-skin contact and cuddling is encouraged. This increased contact results in a demonstrated reduction in the need to treat opioid-exposed infants.[38]

4.3.10 Child Protection

Pregnancy is an ideal time to assess a mother's social situation and to engage her in positive planning for a healthy pregnancy and a healthy baby. Planning should be a coordinated effort, involving the health-care team and patient, as well as supportive family members, community support agencies, and child protection and social workers.

- Once patients have consented to the exchange of information, all necessary health-care providers, including physicians and community-based resources, are encouraged to participate in an integrated process to coordinate care. Advance care planning should result in additional supports for the patient and allow her to play a key role in planning for her and her newborn's care after birth.
- The provincial Ministry for Children and Family Development (MCFD) can be involved in a supportive role during pregnancy with the patient's consent, and this partnership leads to the best outcomes for the infant.
- There is no legal obligation to report any concerns regarding a pregnant woman's care to child protection authorities, including methadone use in pregnancy; however, each patient should be informed that if there are protection concerns, a report will have to be made once the child is born.
- Consideration should be given to other children in the home who may be at risk because of paternal substance use.
- The BC Representative for Children and Youth may also be contacted to support children, youth and families who need help in dealing with the child-serving system. It advocates for vulnerable children and youth up to the age of 18 and is particularly concerned with children in government care.
- The MCFD provides child protection services under provincial child welfare legislation, the *Child, Family and Community Service Act (CFCSA).*
- Section 13 of the *CFCSA* describes the circumstances when a child needs to be protected.

[38] Abrahams RR, Kelly SA, Payne S, Thiessen PN, Mackintosh J, Janssen PA. Rooming-in compared with standard care for newborns of mothers using methadone or heroin. Can Fam Physician. 2007;53:1723–30

- Section 14 of the *CFCSA* describes the health-care professional's duty to report the need for protection. Note that the actual determination of whether an infant is at risk for harm, neglect or abuse can only be done by appropriately authorized individuals.
- Access to medical records for the purpose of assessing the infant's safety by these persons must be in accordance with statutory and legal authority.

5. Patients with Comorbid Conditions

Opioid dependent patients must be screened for specific comorbidities given the prevalence in this patient population. **A specific treatment plan needs to be documented in the physician's overall treatment strategy for these conditions.**

5.1 Hepatitis C

Over 80% of people who inject illicit drugs are hepatitis C positive.[39] All patients considered for MBMT must be tested for hepatitis A, B and C, and serum transaminase levels. Periodic retesting for hepatitis C is indicated when risk-taking behaviours continue.

All patients with chronic hepatitis C infection should be considered candidates for antiviral therapy[40] to include hepatitis C RNA quantitative assay, genotype and liver fibrosis assessment. Flow sheets such as the Liver Function Record should be used to track liver enzymes.

5.1.1 Management issues

Hepatitis C management should focus on the following areas:

1. Lifestyle
    - emphasize abstinence from alcohol
    - discuss appropriate diet
    - advise use of condoms in non-monogamous sexual encounters
    - advise on availability of harm-reduction supplies
2. Immunization
    - vaccinate for hepatitis A and B, and provide other relevant vaccinations
3. Treatment
    - initiate treatment or refer to a physician with expertise in hepatitis C treatment when indicated

[39] Patrick DM, Tyndall MW, Cornelisse PGA, Li K, Sherlock CH, Rekart ML, et al. Incidence of hepatitis C virus infection among injection drug users during an outbreak of HIV infection. CMAJ. 2001;165:889–95.
[40] Myers RP, Shah H, Burak KW, Cooper C, Feld JJ. An update on the management of chronic hepatitis C: 2015 Consensus guidelines from the Canadian Association for the Study of the Liver. Can J Gastroenterol Hepatol. 2015 Jan-Feb;29(1):19-34

- Wherever possible, Hepatitis C treatment should be co-administered with methadone (e.g. DWI) to enhance compliance and treatment success

5.2 HIV/AIDS

People who inject illicit drugs are at high risk for contracting HIV and MBMT is among the best ways to prevent HIV transmission in this population. Some MBMT patients will be HIV positive on entry into treatment or may acquire HIV during treatment, if they continue to engage in other high-risk behaviours.

Among other potential benefits of MBMT, stabilization on methadone or buprenorphine may make it easier for HIV-positive opioid-dependent patients to be enrolled and retained in HIV treatment regimens. Priority access to MBMT should be provided whenever possible for HIV-positive patients because of the individual and public health consequences of untreated HIV infection, especially in the injection drug-using population.

5.2.1 Management Issues

HIV management should focus on the following areas:

1. Education
    - provide education on sexual contact precautions and needle sharing
2. Immunization
    - immunize for hepatitis A and B
    - immunize for tetanus toxoid, pneumococcal vaccine and influenza vaccine
3. Testing and monitoring
    - consider testing for tuberculosis and syphilis
    - monitor CD4 counts and viral load
4. Treatment and referral
    - refer to an infectious disease specialist for assessment and treatment plan
    - HIV medications interact with methadone—dose adjustments may be required and patients should be carefully monitored in collaboration with the pharmacist. A list of medications metabolized by cytochrome P450 3A4 is available here.
    - refer to when possible, HIV treatment should be co-administered with methadone (DWI) to enhance compliance and treatment success

5.3 Mental Health Issues – Concurrent Disorders

Lifetime prevalence for another Axis I co-occurring disorder in substance dependent patients is at least 30%. Depression, anxiety, bipolar disorder, eating disorders and process addictions (compulsive gambling, sexual and internet behaviours, etc.) are common, as are Axis II disorders, and often contribute to continued substance use.

Identifying and providing treatment for patients with mental illness improves MBMT outcomes, such as reducing substance use and improving treatment retention.[41]

5.3.1 Management Issues

The initial assessment should always include screening questions for comorbid mental illnesses. Past psychiatric treatment, a family history of mental illness, and opioid/other drug abstinence periods (at least four to six weeks) are all important considerations when assessing for mental illness independent of substance use.

Often, mental health and substance use coexist as concurrent disorders. Depending on the severity, the patient can be treated either in the primary care/addiction clinic or in a specialist setting. Health Canada's *Best Practices – Concurrent Mental Health and Substances Use Disorders* further outlines guiding principles for the treatment of concurrent disorders.

It may be difficult to determine whether a psychiatric disorder is primary or secondary to substance use disorder. Alcohol, for example, may cause symptoms which present as mental illness (such as bipolar or depression) or may interfere with the management of an underlying mental illness. Opioid withdrawal often presents as increased anxiety, mood instability and in some cases can trigger underlying psychosis. These symptoms tend to subside over a period of approximately 4 weeks, during which careful monitoring and risk assessment is needed. The distinction may be clearer, as in the case of a rapidly resolving psychotic state, on cessation of cocaine or crystal methamphetamine use. In order to differentiate primary from secondary psychiatric disorders, a skilled assessment is required that takes into account symptom progression during substance use and periods of abstinence.

Substance dependent patients also have a significantly higher incidence of mental, physical and sexual abuse. Trauma-informed practice is a standard of care in managing these patients, and the TIP guide is a useful resource for understanding and supporting them.

5.4 Polysubstance Comorbidity

The benefits of MBMT are reduced in the setting of continued psychoactive substance use. Polysubstance misuse (both prescription and illicit) is common among opioid-dependent patients. All patients require a comprehensive assessment that includes a detailed inventory of drug use and an individualized treatment plan.

41 King VL and Brooner RK (1999). Assessment and treatment of comorbid psychiatric disorders. In: Strain EC, Stitzer ML editors. Methadone treatment for opioid dependence. Baltimore: Johns Hopkins University Press. p.141–65.

5.4.1 Management Issues

Stimulants

Patients may still meet criteria for OUD when the drug of choice is a stimulant. Failure to recognize concurrent stimulant-use disorders will undermine methadone/buprenorphine treatment outcomes. A trial of treatment may be appropriate but a stimulant management plan must be in place from the outset. Methadone/buprenorphine treatment should only be continued long-term if objective benefits can be documented.

Alcohol

Alcohol use poses unique concerns in methadone/buprenorphine maintenance patients. The risk of overdose is increased, given the synergistic respiratory depressant effect alcohol has with methadone and buprenorphine. In addition, alcohol interferes with the metabolism of both drugs. In its early stages, problem drinking has the potential to induce hepatic enzymes which can accelerate methadone and buprenorphine metabolism. At later stages, liver failure can precipitously reduce a patient's tolerance to methadone and buprenorphine. These complicated interactions underscore the need for physicians to appropriately screen and monitor for alcohol use disorders and provide intervention and treatment.

Sedative-Hypnotics Including Benzodiazepines and Z Drugs

Comorbid sedative-hypnotic use poses another set of unique challenges. Like alcohol, these drugs have a synergistic respiratory depressant effect when used with methadone or buprenorphine and may increase the risk of fatal overdose. Multidoctoring for sedative-hypnotics is common. It is the responsibility of the prescriber to review PharmaNet profiles regularly. All psychoactive substances act through a final common end pathway in the brain, therefore sedative-hypnotics are relatively contraindicated in patients with substance use disorders.

Marijuana

Continuing use of a psychoactive substance such as marijuana can undermine treatment focused on developing non-chemical coping strategies. While there is controversy as to whether marijuana causes an "amotivational syndrome," there is evidence that psychosis, anxiety and mood disorders, and permanent cognitive changes can occur secondary to chronic marijuana use.

Physicians considering the provision of support for medical marijuana exemption should review the College's standard *Marijuana for Medical Purposes*, and consider marijuana as a treatment of last resort in a patient with a history of substance use disorder.

Tobacco

Tobacco consumption rates are comparatively high for those with addictions to opioids, which means tobacco-related disease and associated mortality are significant long-term risks to their health. Physicians with MBMT patients are encouraged to

- inquire about their tobacco use and advise them to quit

- assist in an attempt to quit (and, if appropriate, offer medication support from the BC Smoking Cessation Program), and
- arrange for follow-up (the QuitNow BC referral program is available to offer behavioural support).

6. Hospitalized Patients

Methadone/buprenorphine maintenance patients are commonly hospitalized. These patients will have to have their methadone prescribed by a physician who has one of the following:

- a full authorization to prescribe methadone for opioid use disorder
- a temporary authorization to prescribe methadone
- a hospitalist authorization, which is a hybrid of a full exemption to prescribe methadone for analgesia and for OUD, for in-hospital use only

Physicians prescribing methadone for hospitalized patients are expected to adjust the dose as clinically indicated. Physicians with temporary or hospitalist methadone authorizations may write bridging methadone prescriptions for patients discharged from hospital. Hospitalist physicians are responsible to ensure that patients have an appointment with a community prescriber before being discharged.

Hospital-based physicians are encouraged to obtain hospitalist authorizations to prescribe methadone. These are granted after physicians attend the College-sponsored Hospitalist Workshop (held in conjunction with the Methadone 101 Workshop) and undergo a brief interview with the deputy registrar.

The role of the hospital-based physician is to:

- determine if methadone/buprenorphine continuation is appropriate
- determine the dose and frequency of administration
- reassess and adjust the dose as clinically indicated
- facilitate transfer of care to the community physician on discharge

The Hospitalist Workshop is offered once or twice a year to educate physicians on the management of hospitalized patients for both opioid use disorder and analgesia.

Management of hospitalized methadone patients should include:

- appropriate patient assessment, including confirmation of current and last dose
- assessment of current substance use, medications and medical conditions affecting methadone or buprenorphine pharmacokinetics

- contact with the community methadone or buprenorphine prescriber
- pain management
- informing community physicians about discharge information

7. Provincial and Federal Corrections Facilities

7.1 Provincial Corrections Facilities

There are nine adult correctional and three youth custody centres in British Columbia, with over 50,000 admissions per year. Health-care services are provided in each centre. All centres but one, a remote camp with limited access to health-care services on weekends, provide for continuation of methadone and buprenorphine-naloxone. All medical information is confidential and restricted to health-care providers only.

Transfer forms are completed upon admission. PharmaNet profiles are reviewed and patients sign a standard BC Corrections methadone patient agreement. BC Corrections advises community physicians by fax when their patients are in custody. An admission UDT is provided for all patients on methadone or buprenorphine-naloxone for maintenance.

Frequency of subsequent testing is individualized and included as part of the treatment plan. Only physicians working within correctional and youth custody facilities are able to prescribe methadone or buprenorphine-naloxone for patients in custody. All physicians working in BC Corrections have current methadone authorization. Methadone or buprenorphine-naloxone doses are individualized by the treating physician and administered by nurses using daily witnessed ingestion protocol. Drug counselling, education and mutual support meetings are available in most centres and participation is strongly encouraged. Due to risk of relapse and overdose among recently incarcerated individuals, overdose prevention counselling and a take-home naloxone prescription upon discharge from a correctional facility are recommended.

When released, MBMT patients are transferred back to a community prescriber. The health-care staff or the patient makes an appointment with the community prescriber. To facilitate transfer of care a short-term DWI prescription is faxed to a pharmacy chosen by the patient. Many inmates are released without notice immediately following their court appearances. In these cases, arrangements for methadone or buprenorphine-naloxone prescriptions and follow-up appointments are exclusively the responsibility of the patient.

7.1.1 Initiation of Methadone or Buprenorphine-naloxone Maintenance Treatment

Initiation of methadone or buprenorphine-naloxone maintenance in provincial correctional facilities is increasing. High volume and short periods of incarceration (generally under 30 days) create challenges for initiation of all inmates who qualify. Patients are selected according to criteria outlined in this guideline, and prioritized according to a triage algorithm. Buprenorphine-naloxone has considerably

increased the number of initiations due to its rapid stabilization ability, and is the drug of choice in BC Corrections.

7.1.2 Drug Treatment Court of Vancouver

The Drug Treatment Court of Vancouver is a voluntary alternative to incarceration available to some offenders charged with drug-related offences. Once accepted into the program, patients receive intensive substance use disorder treatment as well as medical and mental health care. Both methadone and buprenorphine-naloxone initiation and maintenance feature prominently in this program.

7.2 Federal Corrections Facilities

Federal correctional institutions house inmates serving sentences of two years or more, with most sentences exceeding three years. Correctional Service Canada offers comprehensive methadone and buprenorphine-naloxone maintenance treatment programs with extensive mental health, substance use disorder, medical and risk-behaviour assessment. Patients are screened regarding need and suitability for these treatment programs. Methadone and buprenorphine-naloxone initiation are available whenever appropriate, and all inmates already enrolled in the Methadone Maintenance Program are continued on maintenance. Extensive counselling is available and strongly encouraged.

8. Patients Who Wish to Travel

Long-term MBMT limits patients' ability to travel. If patients receiving MBMT wish to travel for a period of time that exceeds their regular carry period, patient and public safety should not be compromised. **Physicians should not authorize carries for patients who are unstable even if patients are planning to travel unless a documented risk-benefit assessment outlines the reasons for granting the carry for travel.**

Physicians who are concerned about prescribing carries for travel should confirm travel plans when possible. Physicians may assist with arrangements for DWI at pharmacies in other locations, but this is not always possible. Physicians may also assist by faxing prescriptions or liaising with the destination pharmacist. PharmaCare will not reimburse patients for prescriptions filled out of province.

Physicians who agree to provide methadone carries for travel may offer patients the option of a prescription for Metadol tablets instead of solution. Metadol tablets are not covered by PharmaCare for OUD and should be prescribed on the regular duplicate prescription form and not the methadone prescription pad.

9. Rural Settings

Despite positive developments in substance use treatment in British Columbia, MBMT provision is unevenly distributed across the province, and need often exceeds capacity in many regions. Some view addiction treatment as a "specialty" and suggest access will necessarily be limited in rural areas. What is clear is that system capacity in rural and remote communities is woefully lacking. Patients residing in rural areas experience multiple barriers in accessing substance use treatment. These stem from the common rural barriers to behavioural health care (cost associated with geographical factors, travel, lack of transportation, social stigma and discrimination, availability of services such as Alcoholics Anonymous, Narcotics Anonymous, counselling) as well as the urbanocentric distribution of substance use treatment facilities, all of which negatively impact access to substance use treatment. Further challenges exist in smaller locales in providing MBMT. Prescribing physicians in rural areas can feel pressured to take on more MBMT clients than they can integrate into their practice due to a lack of prescribing physicians in the area. Many communities do not have a prescribing physician, and some physicians may have to restrict their MBMT caseloads so as not to overwhelm their regular practices.

Providing MBMT services to rural regions will necessarily require more careful attention to service delivery and design than is the norm. In the case of methadone, there can be some specific complications, including, among other issues, how to adequately initiate treatment with appropriate levels of assessment and monitoring, how to dispense methadone, and how to monitor the use of other substances during treatment. Delivering a comprehensive package of optimized MBMT is made more difficult when the prescribing physician is not local. In addition, patients' expectations may not be in alignment with current College guidelines. For example, patients may expect that since they live far from the service location, they do not have to attend regularly for face-to-face visits as frequently as they would otherwise. Patients may also live far from the nearest pharmacy, making daily witness ingestion problematic for the patient. Random urine drug testing may be more challenging when patients are monitored from a distance. In all cases, patient and public safety from diverted medication should be paramount. Caution should be exercised with take-home doses. If the patient is unable to attend for regular appointments or unable to attend to the pharmacy frequently in the face of instability, they may not be appropriate for MBMT and consideration should be given to treatment with naltrexone. Buprenorphine may also be impactful in rural areas, given that methadone prescribers are scarce in these regions and existing local physicians' practices can easily be expanded to include buprenorphine treatment.

In either case, intensive consultation prior to starting MBMT is highly recommended. All contact phone numbers, fax numbers, etc. should be communicated to the patient, and contact information for the patient clearly documented in the chart. Clarification of the expectations of the patient should be discussed at the onset, including discussion about emergency care delivery. Extra vigilance is required for patients who are not in stable recovery. All of these factors combine to make rural delivery of MBMT fraught with increased risk, both to the patient as well as to the prescriber.

9.1 Telemedicine to Remote Regions

It is unclear whether all services being provided via telemedicine in the province are meeting the regulatory requirements and certainly, there is a need to develop guidelines to support safe MBMT services provided through telemedicine, including counselling. Support of a local clinical team, skilled and knowledgeable in MBMT is essential, with an established and reliable point person. Prescribers should develop partnerships with interdisciplinary services in the community to support patients and ensure arrangements with local hospitals and other health-care providers are in place for patients to handle emergencies such as overdose. Good communication with local pharmacy and pharmacists are essential. Prescribers should determine whether pharmacies will accept faxed copies of prescriptions until original can be mailed, prior to initiating treatment. All patients should be assigned a most responsible MBMT physician who should maintain documentation of a roster of active and closed charts. Charts (paper or EMR) should be available in both locations. Face-to-face interaction should be the goal at some point during treatment where possible. Bloodwork should be completed prior to starting MBMT, with results sent to both locations. Supportive counselling or case management should be available on-site to the MBMT patient.

Practising medicine using only electronic communication or across different jurisdictions may affect a physician's liability insurance and they should disclose such information to their liability insurer. Prescribers are advised to follow the College's standard on *Telemedicine*.

9.2 Narcotic Prescribing Via Telemedicine

Narcotic prescribing via telemedicine has additional requirements:

1. The initial assessment is critical in developing a treatment plan, discussing counselling, alternative treatments, expectations of caregivers, expectations of patients
2. Ensure a health-care professional is at the patient end who has personally assessed the patient
3. Be extra vigilant regarding take home doses
4. Exercise caution with increases in dosing, particularly in unstable patients
5. PharmaNet profile should be available at both ends of the consult and documented
6. Ensure reliability of UDT
7. Random UDT important

Increasing access to MBMT in rural communities is an important one; however, working in such environments can be higher risk than a working in an urban setting where support, including from other colleagues, is readily available. Above all else, patient safety and community well-being should be the guiding principle.

METHADONE AND PAIN

The authorization to prescribe methadone for analgesia is separate from the authorization to prescribe methadone for OUD.

Physicians wishing to obtain an exemption under section 56 of the *Controlled Drugs and Substances Act* for an authorization to prescribe methadone for analgesia must follow the BC Methadone Program application process.

Required readings for physicians who prescribe methadone for pain include the *Methadone for Analgesia Guidelines* and the College's Professional Standards and Guidelines on *Safe Prescribing of Drugs with Potential for Misuse/Diversion*, as well as completion of the Canadian Virtual Hospice online module (www.methadone4pain.ca).

BUPRENORPHINE AND PAIN

In Canada, sublingual buprenorphine-naloxone is only approved for use in the treatment of opioid use disorder; therefore, in the absence of OUD its use would be considered off-label.

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