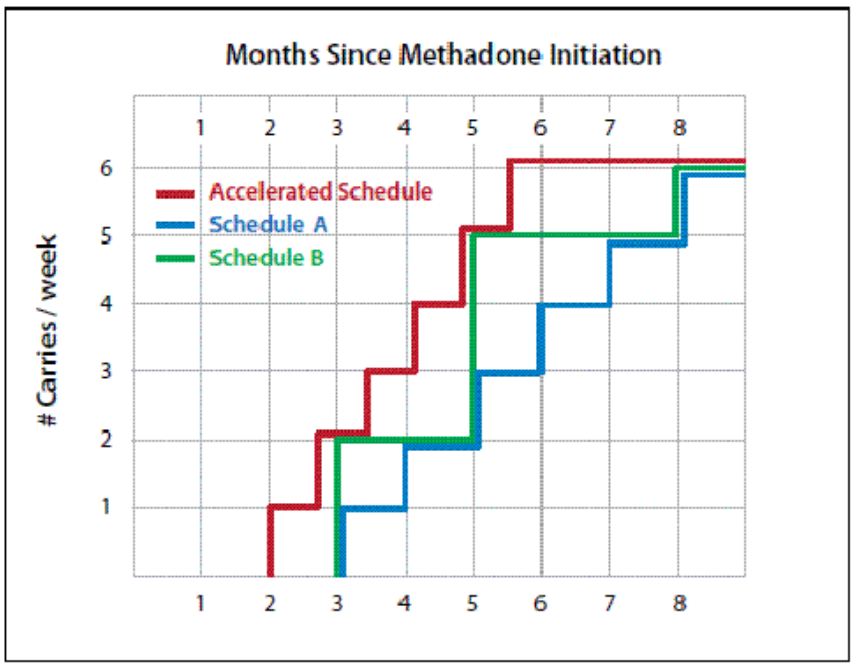
Methadone Maintenance Treatment Standards and Guidelines

April 1 2016

Table of Contents



1. Introduction

1.1 Preface

These Standards and Guidelines are an adaptation of the College of Physicians and Surgeons of Ontario (CPSO) Methadone Maintenance Treatment Program Standards and Guidelines published February 2011 (4th edition) and of the College of Physicians and Surgeons of Nova Scotia (CPSNS) Methadone Maintenance Treatment Handbook published May 2012. Some sections have been adopted with little or no change, some have been adapted with minor or substantial revision, and others have been substantially rewritten. This College gratefully acknowledges the work of the CPSO and the CPSNS, which has served as an invaluable resource in the preparation of these Standards and Guidelines.

1.1.1 Meaning of "Standards"

"Standards" means principles of patient care and management that are generally accepted and recognized by the medical profession in Canada, or that are expressed in a College statement of standards of practice, and that in the case of a College statement of standards of practice may be departed from or modified by a medical practitioner only if ALL of the following conditions are met:

i. The departure or modification is an exceptional circumstance and does not represent the norm for patient management by the medical practitioner;
ii. The departure or modification is limited, in extent and duration, to the minimum necessary to respond to the exceptional circumstance;
iii. The departure or modification, and the reasons for it, are documented in the patient's chart; and
iv. The medical practitioner has complied with any other conditions for departing from the standard set out in the applicable College statement of the standards of practice.

1.1.2 Meaning of "Guidelines"

"Guidelines" means a statement by the College of best practices and recommendations in relation to a particular issue, which may have variable applicability on a case-by-case basis, depending on individual patient circumstances, local resources and the professional judgment of the medical practitioner, and includes College advisories.

The College expects all physicians to document departures from College guidelines appropriately.

1.2 History of MMT in the Treatment of Opioid Dependence

In the early 1900s in the United States, opioid dependence was treated in physicians' offices with morphine. However, as the social issues associated with opioid dependence became increasingly apparent, the government of the day initiated behavioural treatment approaches at "narcotics farms"

and other hospital-like settings that confined and committed addicts to abstinence and presumed recovery. Many of these programs proved costly and ineffective with high post-discharge relapse rates. Pharmacotherapy was a missing component.

During the Second World War, methadone, a long-acting pure mμ agonist, was developed by Bayer in Germany as an analgesic. It was considered to be a non-addictive alternative to morphine. In the 1940s, several studies conducted in the United Kingdom recognized methadone as an efficacious treatment of heroin withdrawal symptoms. In the 1950s and 60s, as opioid use became a serious concern in urban areas with resultant dramatic increases in crime and death rates, researchers and physicians became involved in trying to find a medical solution to opioid dependence. In late 1963 and early 1964, the first methadone study was performed at The Rockefeller Institute for Medical Research by Drs. Dole and Nyswander in an attempt to develop a new pharmacotherapy for opiate dependence (Dole and Nyswander 1965; Dole and Nyswander 1966). Their research concluded that methadone prevented opioid withdrawal symptoms, blocked the euphoria of heroin, and decreased cravings in opioid-dependent individuals and thereby confirmed methadone efficacious as a maintenance medication for opioid dependence.

Meanwhile, it was actually a Canadian researcher, Dr. Robert Halliday from Vancouver, who set up what is believed to be the first MMT program in the world. Since that time, opioid agonist therapy with MMT has become an effective treatment option for opioid-dependent individuals worldwide. In many countries, including Canada, more people are seeking and receiving treatment with MMT.

In Canada, it is estimated that there are more than 80,000 regular illicit opioid users, 30,000 in Ontario (Popova et al. 2006**).** The multisite OPICAN study, with a cohort of regular untreated illicit opioid users from seven Canadian cities surveyed from 2001 until 2005, provides evidence suggesting that heroin has become an increasingly marginal form of drug use among illicit opioid users in Canada, and that instead, prescription opioids in varying forms have become the predominant form of illicit opioid use (Fisher et al. 2005)**.** A chart review of new admissions (1997-1999) to the MMT program at the Centre for Addiction and Mental Health (CAMH) revealed that 83% of patients had used prescription opioids ± heroin (Brands et al. 2004)**.** Also, between 1990 and 1994, there was a significant rise in individuals addicted to controlled-release oxycodone seeking treatment at CAMH (Sproule et al. 2009). The semi-synthetic oxycodone and full synthetic fentanyl have been linked to several deaths in Ontario (Dhalla 2009, Martin et al. 2006)**.**

Literature on the effectiveness of MMT in the treatment of prescription opioid addiction is sparse. Banta-Green, et al. reported that prescription opioid users can be treated at least as effectively as heroin users in MMT (Banta-Green et al. 2009). Prescription-opioid users often have pain problems and obtain their opioids legally from a prescriber indicating that they were still under medical supervision for their pain; these patients were more likely to have psychiatric treatment and take sedatives/anxiolytics or antidepressants (Brands et al. 2004).

MMT is based on a harm reduction philosophy and represents one component of a continuum of treatment approaches for opioid-dependent individuals. MMT is a substitution therapy that allows a return-to-normal physiological, psychological and societal functioning. It is one possible treatment for opioid dependence. For some people, MMT may continue for life, while others may be able to eventually discontinue MMT and remain abstinent while preserving the normal level of function they attained while on MMT. Each patient must be assessed, treated, and monitored on an individual

basis. Successful outcomes through MMT require knowledge, experience, vigilance, and diligence on the part of the MMT physician, the patient, and all of those involved in treatment.

Methadone alone does not constitute effective treatment of opioid dependency. Effective MMT services would ideally comprise the following components:

- an appropriate methadone dose
- routine medical care
- treatment for other substance dependence
- counseling and support
- mental health services
- health promotion, disease prevention and education
- linkages to other community-based services
- outreach and advocacy.

The College recognizes that not all of these components may be readily available to patients in all communities or within a timely manner throughout our province. MMT providers must ensure that patients are aware of the services available to them.

1.3 Effectiveness of Methadone

Methadone has been extensively researched for safety and its efficacy to reduce morbidity and mortality in opioid dependent patients. The research data and medical literature shows that:

- MMT reduces morbidity and mortality associated with heroin addiction (Gunne and Gronbladh 1981; Kinlock et al. 2009; Newman and Whitehill 1979; Strain et al. 1993).One study found that patients were three times as likely to die without MMT than if they were maintained on treatment (Caplehorn et al. 1994). In addition, studies have shown that MMT can indirectly decrease mortality by decreasing the risk of HIV infection while on MMT (Ball et al. 1988; Caplehorn and Ross 1995). A Cochrane review (Mattick et al. 2009) of 11 randomized clinical trials found that methadone was more effective than non-pharmacological treatments with respect to the outcomes of treatment retention and suppression of heroin use. The great majority of trials were with heroin users.

- There is evidence that MMT reduces illicit opioid and other drug use (Gunne and Gronbladh 1981; Kinlock et al. 2009; Yancovitz et al. 1991). For example, an early trial found that compared to methadone, the control group was more than three times likely to test positive for heroin use at a one-month follow-up after treatment (Yancovitz et al. 1991). MMT also reduces other substance use. One large prospective study (Fairbank et al. 1993) of methadone patients found a reduction in the use of cocaine, amphetamines, illegal methadone, sedatives, and marijuana at follow-up. Other factors associated with decreased drug use include counseling, adequate dosing, contingency management strategies such as take-home doses, and harm reduction program orientation (Kletter 2003; Kraft et al. 1997; Ling et al. 1996; McLellan et al. 1993; Stitzer et al. 1992; Villano et al. 2002).

- There remain few studies on the effectiveness of MMT for prescription opioid (PO) abuse and dependence.

- Methadone is a receptor agonist with pharmacological properties similar to those of morphine. It exists as two isomers (d and 1 forms) but it is believed that most of the analgesic activity resides in the one isomer (Scott et al. 1948). However, most of the methadone used in clinics is a racemic mixture. Methadone has ideal properties for a maintenance agent: it is orally active and long-acting (one dose suppresses symptoms of opioid withdrawal for 24-36 hours without producing euphoria, sedation and analgesia). This enables patients to function normally (i.e without impairment) and experience normal pain and emotional responses. Another advantage of .methadone is the ability to suppress craving (Lowinson et al. 2005).

Methadone is well absorbed after oral administration and levels are detectable at 30 minutes with peak concentrations occurring at four (4) hours and it is 90% bound to plasma protMethadone is extensively metabolized in the liver to pyrrolidines and pyrroline (via *N*-demethylation and cyclization) which are then excreted in urine and bile (Gutstein and Akil, 2006). The elimination half-life ($t_{1/2}$) of methadone is approximately 22 hours but there is considerable inter-individual variability and estimates range from 5-130 hours (Eap et al. 2002).

1.4 Conclusion

The medical literature supports that MMT is a well-established and cost-effective treatment paradigm. MMT saves lives and reduces drug use as well as the transmission of HIV, Hepatitis C, and other communicable diseases. The effectiveness of MMT is enhanced with contingency management and counseling.

2. MMT Physicians and Practice Settings

MMT is prescribed in different settings using many different models of care

2.1 Overview

MMT may be prescribed in different settings, using different models of care such as: primary care, MMT focused practices, community-based agencies, hospitals, medical detox units (DTU), residential addiction treatment centres, and correctional facilities. This section outlines the requirements of all MMT prescribers in these practice settings.

2.1.1 Standards

The MMT physician shall complete:

1. the Opioid Dependence Treatment Core Course prior to obtaining a methadone exemption; and
2. the full Opioid Dependence Certificate Program within 3 years of receiving an exemption.

2.1.2 Guidelines

None for this section.

2.2 Obtaining a Methadone Exemption

For an exemption to prescribe MMT, a physician must:

- Hold a license to practice in Newfoundland and Labrador
- Be in good standing with the CPSNL
- Complete an application form and agree to practice in accordance with the CPSNL's expectation document
- Complete the Opioid Dependence Treatment Core Course through CAMH, or equivalent program acceptable to CPSNL
- Complete two days of clinical training with a MMT physician approved by the CPSNL.

The initial exemption is issued for one year with subsequent exemptions issued every three years. For more information contact CPSNL.

2.3 MMT Physician Practice Settings

2.3.1 Primary Care MMT Practice

General practitioners and family physicians may provide MMT in solo medical practice or group practices such as primary health care teams, private medical clinics, hospital-based health clinics and community-based health centers, including chronic care centers. They may prescribe methadone either integrated with or separate from their medical practice. Some

MMT patients in Newfoundland and Labrador receive medical care as well as MMT from their primary-care physician. Some physicians in private practice provide psychotherapy as well as MMT and other medical services.

MMT based in primary practice has several advantages, such as being less stigmatizing and addressing previously unmet medical needs (Fiellin et al. 2001; King et al. 2002; Lewis and Bellis 2001; Merrill et al. 2005). However, patients may have to travel to receive pharmacy, laboratory, and other specialized addiction and support services. Group practices may have advantages over solo practice. Research by Strike et al. (2005) indicates that group practices may have better retention rates than solo practitioners and the integration of primary-care services within group practices is likely to lead to better outcomes for MMT patients.

2.3.2 MMT-Focused Practice

MMT physicians who work in focused methadone clinics (both outpatient and inpatient) may be general practitioners, family physicians, or Royal College of Physicians and Surgeons Specialists. Such physicians may have additional training or exam certification in Addiction Medicine and focus their clinical practices in MMT; their practices may consist entirely or predominantly of MMT patients.

MMT physicians in focused practices may not provide primary care to their patients. Patients may need to seek out primary care or psychosocial services in the community.

2.3.3 Community-Based MMT Practice

Community-based physicians may provide services through publicly funded, community based clinics that integrate psychosocial care. Community-based clinics operate under a harm-reduction philosophy and involve a multi-disciplinary team (social workers, nurses, case managers, dieticians, pharmacists) in the patient's care.

These clinics usually offer a comprehensive MMT program that includes health and social supports. This kind of one-stop clinic model saves time and expenses for the patient and addresses the patients' quality of life issues. It also helps to ensure coordination and communication among the service providers.

2.3.4 Hospital and Corrections-Based MMT Practice

MMT physicians in hospitals and some residential addiction-treatment centres may maintain patients on their community-based MMT program or may initiate MMT in some circumstances.

Hospital-based physicians providing care for MMT patients may apply for temporary methadone exemptions, one patient at a time, to manage admitted medical, surgical, and psychiatric patients. They may not have specialized knowledge of opioid dependence (see Section 14 Hospital-Based MMT).

Correctional facilities manage many patients with opioid dependence and may provide MMT (see Section 13: MMT in Federal/Provincial Correctional Facilities).

3. Options other than MMT for Opioid Dependence

The main treatment options for opioid dependence are abstinence-based treatments and opioid agonist therapy (also known as opioid substitution therapy) with methadone or buprenorphine

3.1 Overview

The main treatment options for opioid dependence are abstinence based treatments and opioid agonist therapy (also known as opioid substitution therapy) with methadone or buprenorphine. MMT physicians must be familiar with the indications, benefits, and risks of each option, in order to provide the safest and most effective treatment for their patients. This section briefly reviews options other than MMT. Physicians contemplating these options should consult with appropriate addiction treatment resources.

3.1.1 Standards

1. The MMT physician shall inform the patient of all appropriate and available treatment options to treat opioid dependence, including risks and benefits, so that the patient may make an informed decision about the use of MMT prior to initiation.
2. Physicians who prescribe buprenorphine shall have the appropriate knowledge, skills, and judgment to do so, demonstrated by completion of the CAMH Opioid Dependence Core Course (or equivalent program acceptable to CPSNL).
3. In order to prescribe buprenorphine, a methadone exemption for opioid dependence is required by the College.
4. Physicians planning to prescribe buprenorphine shall also complete the on-line buprenorphine CME Course or equivalent.
5. Patients shall be warned that after detoxification:
    i. their tolerance to opioids will go down putting them at risk for overdose if they relapse to their usual opioid dose; and
    ii. the emotional distress associated with opioid withdrawal may increase the risk of suicidal ideation.

3.1.2 Guidelines

1. The MMT physician should be familiar with the individual patient factors to be taken into consideration in the choice for buprenorphine as an opioid agonist therapy.
2. MMT physicians should take appropriate precautions to avoid the adverse outcomes described in Standard 3.1.1(5) above.

3.2 Abstinence Based Treatments

Abstinence based treatment may consist of medically supervised withdrawal from opioids, followed by an inpatient or outpatient psychosocial treatment program, and/or 12 Step group participation

(AA, CA, NA). While abstinence based treatment may be less effective than MMT, patients may prefer a trial of abstinence before committing to long-term opioid agonist therapy (Richman et al. 1972).

Experience reveals that the proportion of opioid addicts who successfully complete detoxification tends to be low, while the rates of relapse to opioid use following detoxification are relatively high.

Patients should be warned that after detoxification 1) as a result of losing their tolerance to opioids, they are at risk for overdose if they relapse to their usual opioid dose, and 2) emotional distress associated with opioid withdrawal may increase the risk of suicidal ideation. MMT physicians should take appropriate precautions to avoid these adverse outcomes.

3.2.1 Indications for Abstinence Based Treatment

Patient preference. Many patients prefer a trial of detoxification first, as some view opioid agonist treatment as inconvenient and time consuming.

Prior sustained response to abstinence based treatment. Patients may consider re-trying abstinence based treatment if they previously maintained a long period of abstinence following psychosocial treatment.

Good prognostic factors. Patients may be more prepared for medically supported withdrawal followed by abstinence if they are highly motivated for change and opioid abstinence, and have good prognostic factors for recovery from addiction. (e.g., socially stable, supportive social network, short duration of addiction, no major psychiatric co-morbidity, not addicted to other drugs) (Gossop et al. 1989; 1990; Rabinowitz et al. 1997; Unnithan et al. 1992; Washton et al. 1984).

3.2.2 Pharmacotherapy for the Systematic Treatment of Opioid Withdrawal

The most common drugs used to alleviate opioid withdrawal symptoms are alpha adrenergic agonist (e.g., clonidine), and opioid agonists (e.g., methadone and buprenorphine). See table below. Buprenorphine tapering is substantially more effective than clonidine and other non-opioid treatments in reducing opioid withdrawal symptoms and retaining patients in treatment (see Table 01: Withdrawal Management).

Table 01: Withdrawal Management

Drug	Dose	Opioid Withdrawal Symptoms
Buprenorphine	Initial dose 4-8 mg a day sublingually Increase by 2-4 mg a day until therapeutic dose (usual range 8-16 mg) Inpatient: reduce by 2 mg every 1 to 3 days Outpatient: reduce by 2 mg every week	Most withdrawal symptoms
Clonidine	0.1 mg 1–2 tabs p.o. b.i.d.to q.i.d. p.r.n.	agitation, diaphoresis, and sympathetic overdrive
Dimenhydrinate	50 mg p.o. or p.r. p.r.n.	nausea
Ibuprofen	200 mg 1–2 tabs p.o. t.i.d. p.r.n.	myalgia
Immodium	2 mg p.o. p.r.n. (maximum 6 tabs/day)	diarrhea stool
Trazodone	50–100 mg p.o. q.h.s. p.r.n.	insomnia
Benzodiazepines	p.r.n. at MMT physician's discretion **Caution: risk of respiratory depression and death**	anxiety

Cautions for use of clonidine:

1. Do not prescribe clonidine if blood pressure (BP) <90/60, or if the patient is pregnant, on antihypertensives or has heart disease.
2. Warn patients about postural symptoms and drowsiness. Postural symptoms are dose-related, so be cautious with higher doses.
3. Warn patients about mixing with opioids, or having prolonged hot bath (both can cause hypotension).
4. Do not prescribe for longer than 2 weeks (rebound hypertension).

3.3 Opioid Agonist Treatment

3.3.1 Buprenorphine Treatment

Long-acting opioids used in the treatment of opioid dependence include buprenorphine and methadone. While this document focuses on the use of methadone, this section briefly introduces the use of buprenorphine. References such as the CAMH document *Buprenorphine/Naloxone for Opioid Dependence: Clinical Practice Guidelines* may serve as a helpful resource. Download CAMH Guideline: http://knowledgex.camh.net/primary_care/guidelines_materials/Documents/buprenorphine_naloxone_gdlns2012.pdf

Buprenorphine/naloxone (Suboxone) is a sublingual partial mμ agonist that relieves withdrawal symptoms and cravings for 24 hours or more when administered in appropriate doses. Suboxone combines buprenorphine (a partial agonist), which is an effective therapy for opioid dependence, and naloxone (an opioid antagonist), which is intended to limit intravenous misuse and the potential for diversion. The naloxone component of Suboxone has limited sublingual and oral bioavailability and is inactive when Suboxone is taken as prescribed.

Because it has a ceiling effect, buprenorphine appears to be safer in overdose compared to methadone. However, buprenorphine may also be somewhat less effective than methadone at retaining patients in treatment.

The maximum dose for buprenorphine (24 mg) is probably less effective than methadone at doses above 60 or 80 mg; therefore, methadone may be more appropriate for patients who are dependent on large doses of opioids. Patients who have failed at buprenorphine treatment may be switched to MMT; switching from methadone to buprenorphine is clinically more difficult. MMT is considered first-line therapy.

3.3.2 Indications for Buprenorphine Treatment

Buprenorphine can be used for opioid addiction in situations where MMT has failed or where contraindications exist:

- Patients with prolonged QTc interval secondary to methadone treatment or any other cause
- Patients who are unable to tolerate methadone
- Patients who have failed methadone maintenance treatment

3.3.3 Buprenorphine: Practical Issues

- In Canada, buprenorphine is available as Suboxone®, a buprenorphine/naloxone combination product.
- As with other opioids, buprenorphine is subject to the federal Controlled Drugs and Substances Act.
- Access to buprenorphine may be limited for some patients, as Suboxone is not covered by the Newfoundland and Labrador Prescription Drug Plan (NLPDP).
- Physicians are not required to notify CPSNL of the names of patients prescribed buprenorphine.
- Physicians who prescribe buprenorphine shall have the appropriate knowledge, skills, and judgment to do so, demonstrated by completion of the CAMH Opioid Dependence Core Course (or equivalent program acceptable to CPSNL).
- In order to prescribe buprenorphine, a methadone exemption for opioid dependence is required by the College (see Standard 3.1.1(3)).

A guideline for the prescribing of buprenorphine has been developed by the CPSNL and is available through the College's website. CPSNL Buprenorphine guideline: http://www.cpsnl.ca/default.asp?com=Policies&m=340&y=&id=63

For any further information about training in buprenorphine prescribing, contact CAMH at (416) 535-8501 or www.camh.net.

3.4 Conclusion

Table 02

Consideration of Factors for Buprenorphine vs Methadone vs Abstinence-based Treatment

Abstinence-based treatment	Buprenorphine	Methadone
• Patient preference • Good prognostic factors • Has not tried abstinence-based treatment • Had a prolonged period of abstinence following previous abstinence-based treatment	• Failed or had adverse effects with methadone • Quickly relapsed after withdrawal management • Good prognosis; may not need long-term opioid agonist treatment • At higher risk for methadone toxicity	• Failed or had adverse effects with buprenorphine • Quickly relapsed after withdrawal management • Intravenous buprenorphine abuse • High risk for treatment drop-out

4. Initial Patient Assessment

A comprehensive assessment is necessary to make an accurate diagnosis and ensure an appropriate treatment plan.

4.1 Overview

Initial patient assessment for MMT involves assessing for suitability for MMT, a history and brief physical examination, urine drug screening and other investigations, and a discussion and review of treatment options and necessary documents pertinent to MMT.

4.1.1 Standards

1. The MMT physician shall establish that the patient meets the DSM IV criteria for opioid dependence prior to MMT initiation (see Appendix A: Diagnostic Criteria for Substance Dependence).
2. The MMT physician shall be knowledgeable of any potential risks for methadone toxicity prior to MMT initiation and manage the patient's care appropriately.
3. The MMT physician shall ensure there has been a discussion with the patient about potential issues with methadone prior to initiation of MMT (i.e. discussion of side effects, risks, and difficulty withdrawing from and tapering off methadone.)
4. The MMT physician shall have a Methadone Maintenance Treatment Agreement signed by the patient and documented in the chart, using the Appendix D: Methadone Maintenance Treatment Agreement format. See also Section 4.4.2 for further information.
5. The MMT physician shall obtain and interpret a urine drug screen (UDS) prior to MMT initiation.
6. If an initial UDS is positive for EDDP , the MMT physician shall verify the source of methadon*e* with the patient (such as non-prescribed or obtained by prescription in another province).
7. Physicians shall use a Physician Pharmacist Treatment Agreement letter (Appendix G). The Treatment Agreement shall be signed within two weeks of initiating MMT.

4.1.2 Guidelines

1. The MMT physician should consider abstinence based treatment and/or opioid substitution for withdrawal purposes for patients with a shorter duration of opioid dependence, i.e less than one year.
2. The MMT physician should consider MMT for patients only after a thorough assessment and discussion about all appropriate and available treatment options. The MMT physician should obtain from the patient the information identified in the Appendix C: Initial Patient Assessment Form, and should assist the patient in identifying what drugs should be included in their drug history.

3. With patients under 19 years of age, the MMT physician should consider, where appropriate and in accordance with CPSNL's Guideline on Consent to Medical Treatment of Minors (http://www.cpsnl.ca/default.asp?com=Policies&m=340&y=&id=11) discussing with other family members potential issues with methadone including side effects, risks and difficulty withdrawing and tapering off of methadone.
4. The MMT physician should seek and document consultations with an experienced methadone provider prior to initiating a patient under 19 years of age on MMT.
5. For all patients that may be initiated on MMT, the physician should document the following in addition to a medical history:
    a. pattern of use of all major drug classes (including tobacco and alcohol)
    b. addiction treatment history and response
    c. high-risk behaviour, such as needle sharing and sex trading
    d. psychiatric history, current mental status (particularly suicidal ideation)
    e. social situation (including child custody and the partner's drug use history)
    f. details regarding chronic or recurrent pain
    g. observable signs of withdrawal.
6. The MMT physician should conduct, or arrange for, a focused physical examination prior to initiating MMT or within a reasonable amount of time (i.e. during the early stabilization phase).
7. The MMT physician should request, or arrange to be requested by the primary care physician, blood work which includes HIV, and hepatitis B and C serology during the early stabilization phase or within a reasonable amount of time after initiation on MMT (i.e. within 15 days).
8. The MMT physician should test, or arrange for the primary care physician to test, for pregnancy in female patients of childbearing potential prior to initiating MMT or within a reasonable amount of time after initiation on MMT (i.e. within 15 days).

4.2 Criteria for MMT

The MMT physician should consider the following criteria for MMT prior to initiation:

1. Opioid use (a urine drug screen that is positive for opioids and verifies the patient's history) (**Note that obtaining and interpreting a UDS prior to MMT initiation is a Standard under Section 4.1.1)**.
2. Meets DSM IV criteria for opioid dependence (See Appendix A: Diagnostic Criteria for Substance Dependence). **(Note that this is a Standard under Section 4.1.1).**
3. Lower likelihood of benefit from non-MMT treatments.
4. No contraindications to MMT.

5. Agreement to terms and conditions of the MMT program. **(Note that an Appendix D Methadone Maintenance Treatment Agreement is a Standard under Section 4.1.1).**

Table 3: Contraindications

Absolute Contraindications	Relative Contraindications
• Hypersensitivity to methadone • Significant respiratory compromise • Paralytic ileus	Use with caution in patients with: • Cardiac conduction abnormalities • Chronic conditions accompanied by hypoxia, hypercapnea or decreased respiratory reserve

Patients may be suitable candidates for MMT even if it was unsuccessful or discontinued in the past. The MMT physician should ensure that there has been a discussion with the patient about potential issues with methadone including side effects, risks, and difficulty of tapering off.

4.2.1 Adolescents

Patients under 19 years of age may be considered for MMT, however abstinence based treatment and/or opioid substitution tapering should also be considered for adolescents, particularly those with a shorter duration of opioid dependence. Any treatment option involving withdrawal should be avoided if the patient is pregnant.

Methadone should be considered after a thorough assessment and a discussion about all appropriate and available treatment options has taken place. The MMT physician shall have a discussion with the adolescent (and other family members where possible) about potential issues with methadone including side effects, risks and difficulty of tapering off.

In cases where a MMT physician considers it appropriate to offer an adolescent MMT, it is recommended that the MMT physician should seek assistance by referral and may request a consultation (formal or informal) with another MMT physician.

Currently, there is a lack of evidence on the effectiveness of MMT in adolescents. However, several studies in the United States are investigating the use of buprenorphine-naloxone in opioid dependent youth (Chakrabarti et al.; Polsky et al. 2010; Subramaniam et al. 2009).

4.3 Assessing a Patient for MMT Initiation

4.3.1 Patient History

There are a number of important areas to concentrate on with regard to patient history for this population of patients. See Appendix C: Initial Patient Assessment Form:

1. Ensure the patient meets the DSM IV criteria for opioid dependence prior to MMT initiation. (See Appendix A: Diagnostic Criteria for Substance Dependence)
2. Identify any potential risks for methadone toxicity prior to MMT initiation (see Table 04: Patient Factors that Increase Risk of Methadone Toxicity)
3. Pattern of use of all major drug classes (including tobacco and alcohol).
4. Previous addiction treatment history and response.
5. High-risk behaviour such as needle sharing and sex trading.
6. Psychiatric history and current mental status including suicidal ideation.
7. Social situation including housing, supports, child custody, and partner's drug-use history.
8. Screen for Behavioural Addictions (See Appendix O: Behavioural Addictions).
9. Details regarding chronic or recurrent pain.

Table 04: Patient Factors that Increase Risk of Methadone Toxicity

High Risk Patients
Recent benzodiazepine use
Use of other sedating drugs
Alcohol-dependent patients
Over 60 years old
Respiratory Illnesses
Taking drugs that inhibit methadone metabolism
Lower opioid tolerance
Decompensated hepatic disease
Recent discharge from inpatient rehabilitation facility
Recent incarceration

4.3.2 Age and Gender

One study showed that older adult MMT patients (> 55 years old) were more likely to report alcohol use and in general, their quality of life did not improve with aging and length of tenure in MMT (Rajaratnam et al. 2009). Firoz and Carlson did not find any differences between MMT patients older than 55 years and their younger counterparts in terms of medical, psychiatric or employment problems (Firoz and Carlson 2004). Schroeder et al provided strong evidence on the significantly higher rates of adverse events (infections, gastrointestinal, musculoskeletal) among female MMT patients, while participants over age 40 reported lower rates of adverse events (Schroeder et al. 2005). Tuchman reported that close correspondence of menopausal symptoms and opiate withdrawal/methadone symptoms could result in inadequate medical attention to problems related to methadone maintenance (Tuchman 2007; 2010).

4.3.3 Focused Physical Examination

The MMT physician should conduct, or arrange for another physician to conduct, a focused physical examination prior to initiating MMT or within a reasonable amount of time (i.e., during the early stabilization phase). Special attention should be given to signs of opioid withdrawal, malnutrition, jaundice, hepatosplenomegaly, cardiovascular and respiratory status, pupil size, needle tracks, and abscesses.

4.3.4 Assessment for Torsades de Pointes Risk Factors

Particular attention must be paid to risk factors for Torsades de Pointes including:

1. The use of cocaine and other stimulants
2. Heavy alcohol consumption
3. Cardiomyopathy
4. Previous MI or valvular abnormalities
5. Family history of long QTc syndrome
6. Liver dysfunction
7. Electrolyte disturbances
8. Medications that affect methadone levels or the QTc interval. (See Table 08: Risk Factors for QTc Prolongation in Patients on Methadone)

4.3.5 Urine Drug Screening (UDS)

Initial urine drug screening facilitates objective corroboration of the patient history of opioid drug use. Some particular UDS results need to be taken into consideration prior to MMT initiation.

4.3.5.1 Initial Opioid Positive Urine without Differentiating/Identifying the Specific Opioid

A patient may be appropriate for initiation on methadone even if their initial urine drug screen is positive for opioids, but does not identify the specific opioid that the patient has reported as their opioid of abuse, if the following circumstances are met:

1. the patient has signs and symptoms of obvious opioid withdrawal OR
2. the patient has obvious track marks OR
3. the patient has been on previous MMT OR
4. the physician has corroborating information from a previous opioid prescribing physician.

4.3.5.2 Initial Opioid Negative Urine

A patient may be appropriate for initiation on methadone even if their initial urine drug screen is negative for opioids, if any of the following circumstances are met:

1. The patient has signs and symptoms of obvious opioid withdrawal OR
2. The patient has obvious track marks OR

3. The patient has been on previous MMT (discuss inconsistency with patient)

4.3.5.3 Methadone-Positive Initial UDS

There are many patients who come for an initial assessment for MMT who have previously tried/used methadone that was not prescribed for them. With a positive initial UDS for methadone or EDDP (a methadone metabolite), it is important to document the patient's history of methadone use.

4.3.6 Other Tests

In addition to UDS, the MMT physician should request bloodwork for HIV, Hepatitis B and C serology and any other relevant bloodwork during the early stabilization phase or within a reasonable amount of time after initiation on MMT. Occasionally, patients refuse or will not comply with this directive. The MMT physician should discuss the concerns with the patient and document the discussion.

In females of childbearing potential, a urine pregnancy test should be done prior to initiating MMT.

4.3.7 Recording Assessments on Subsequent Visits

It is recommended that physicians use the Appendix H: Sample Addiction Medicine Clinical Notes to record assessments on subsequent visits.

4.4 MMT Program Documentation

4.4.1 Notification of CPSNL

As of April 1, 2016, the CPSNL no longer maintains a MMT Patient Registry and therefore does not require notification to the College prior to MMT initiation. However, to avoid MMT duplication and toxicity and/or risk of diversion, patients may not receive a prescription for methadone from more than one physician at a time ("double doctoring").

If a patient seeking initiation of MMT will not sign the Appendix D Methadone Maintenance Treatment Agreement then the MMT physician shall not initiate MMT. The College does not expect that there is any extraordinary circumstance that would reasonably justify a departure from this Standard in the case of initiation of MMT.

In the case of an EDDP/methadone negative initial urine drug screen, a clinical decision may be made by the MMT physician to initiate MMT if there is a concern that a delay in initiation will cause the patient undue harm or cause the patient to drop out of treatment, and provided this is documented by the MMT physician as an extraordinary circumstance.

If a patient seeking continuation of MMT will not sign the Appendix D Methadone Maintenance Treatment Agreement then the MMT physician shall not initiate MMT, unless the MMT physician believes that there is an exceptional circumstance.

4.4.2 Physician Patient Treatment Agreement

Written Treatment Agreements are documents that list expectations of involvement in a MMT program. The use of treatment agreements in MMT programs has proven beneficial to both the patient and the MMT physician. A signed Treatment Agreement is a documentation of informed consent of the patient (see Appendix D: Methadone Maintenance Treatment Agreement). The physician should also, in addition to having the Treatment Agreement signed by the patient, document in their chart that a consent discussion has taken place with the patient, including a discussion of the material risks and benefits of MMT.

The Treatment Agreement includes:

- Patient and provider roles and responsibilities
- MMT program expectations and structure
- Doctor patient confidentiality and exceptions to this
- Expectations of communication with other appropriate providers (pharmacist, treating primary care physicians and consultants)
- General consent (e.g., access to patient charts for MMT physician assessment of their MMT practice).
- Description of risks and benefits.

4.4.3 Physician Pharmacist Treatment Agreement

The MMT physician should communicate his/her expectations with the pharmacist at pharmacies where their patient's methadone is dispensed. This should be accomplished as follows:

1. By the Physician-Pharmacist Treatment Agreement Letter (see Appendix G). The Agreement Letter should outline to the pharmacist details of your treatment agreement with your patient along with your expectations regarding missed doses and intoxication. This must also include providing your contact information for use by the pharmacist in situations where contacting the physician is required by the pharmacy standards of practice or in the case of an emergency.
2. It is recommended that the physician also follow up with a verbal discussion with the pharmacist outlining the details of the MMT physician treatment agreement with the MMT patient along with the MMT physician's expectations regarding missed doses, intoxication.

5. Dosing During Initiation, Stabilization and Maintenance

Patients are at a high risk of death from methadone overdose in the first two weeks of MMT

5.1 Overview

Patients are at a high risk of death from methadone overdose in the first two weeks of MMT**.** Recent prospective population studies from the UK and Australia have revealed that during the first two weeks of methadone treatment the crude mortality rate was 17 per 1000 person years (Cornish et al. 2010; Degenhardt et al. 2009). The risk of fatal methadone overdose during this time period is estimated to be 6.7 times higher than that of heroin addicts not in treatment, and 98 times higher than that of patients on maintenance doses of methadone in treatment for longer periods (Caplehorn and Drummer 1999). A single day's MMT dose can be lethal to non-tolerant individuals. (Harding-Pink, D 1993)**.** The ratio between the maximum recommended initial dose (30 mg) and a potentially fatal single dose is exceedingly narrow compared to other medications (Repchinsky 2003; Wolff 2002)**.**

The prolonged half-life (as long as 55 hours in methadone naïve individuals) and slow bioaccumulation of methadone accounts for its insidious onset of overdose. During dose increases, serum levels accumulate over several days even if the dose is kept the same. Therefore, a dose that is barely adequate on day one can be toxic by day 3-5. This is particularly relevant during initiation on MMT. The patient may appear relatively alert during the day succumbing to an overdose during a nap or at night. Early signs of toxicity include ataxia, slurred speech, "nodding off," and emotional inability (Caplehorn and Drummer 2002).

Concurrent use of benzodiazepines, alcohol, and other sedating drugs substantially increases the risk of death from methadone toxicity. One study found evidence of polydrug use in 92% of methadone-related deaths (Zador and Sunjic 2000). Animal studies indicate that benzodiazepine use substantially increases the risk of fatal overdose (Caplehorn, JR and Drummer, OH, 2002.)

For the purposes of this document, the use of methadone for the treatment of opioid dependency consists of three distinct phases:

Stage 1: *Early Stabilization:* the initial period of MMT (0 – 2 weeks) when the dose is increased safely but rapidly enough to minimize significant withdrawal symptoms (see Section 5.4 and Section 5.5).

Stage 2: *Late Stabilization*: period during which the stable dose is being approached (2 – 6 weeks) (see Section 5.6).

Stage 3: *Maintenance*: when a stable dose has been reached (6 + weeks) (see Section 5.7).

5.1.1 Standards

1. On the methadone prescription, the MMT physician shall specify:
    a. Start and end dates
    b. Days of week that are to be supervised (witnessed ingestion)

c. Number of take-home doses and days of week that are to be given as take-home doses (when applicable)

d. The dose written in numbers and words

e. The daily dose to be mixed in Tang or other crystalline juice to a consistent volume (100 ml is the standard, unless the MMT physician communicates otherwise to the pharmacist).

See Appendix F: Sample Methadone Prescription

2. The MMT physician shall counsel the patient on strategies to avoid methadone toxicity.
3. The MMT physician shall ensure the reason for all dosage adjustments are documented.
4. The MMT physician shall assess the patient in person, or by use of the provincial telehealth network if available for this purpose, prior to each dose adjustment.
5. Dosages should only be increased after the patient has been assessed in person or by use of the provincial telehealth network, if available for this purpose, and it is determined that the patient is experiencing cravings or ongoing opioid use, and/or a constellation of withdrawal symptoms.
6. The MMT physician shall ensure that the starting methadone dose for all patients is 30 mg or less.
7. The MMT physician shall ensure that the starting methadone dose for patients at higher risk for methadone toxicity is 20 mg or less.
8. The MMT physician shall ensure that the starting methadone dose for patients who have been recently abstinent from opioids is 10 mg or less.
9. Subject to the requirement for more frequent assessment under Standard 5.1.1(4) and (5), the MMT physician shall assess the patient at least weekly during early stabilization. See Section 5.3.2
10. For patients who are not at higher risk for methadone toxicity, the MMT physician shall prescribe dose increases of no more than 10-15 mg every 3-5 days during the early and late stabilization phases.
11. For patients at higher risk of methadone toxicity, the MMT physician shall prescribe dose increases of no more than 5-10 mg every 3-5 days during the early and late stabilization phases.
12. For patients who have recently been abstinent from opioids for seven or more days, the MMT physician shall prescribe dose increases of no more than 5 mg every five or more days during the early and late stabilization phases.
13. The MMT physician shall not increase the patient's dose more than 10 mg every 5-7 days during the maintenance phase or once the patient has reached a dose of 80 mg.
14. If the patient misses two or more consecutive doses during the early stabilization phase, the MMT physician shall cancel all subsequent doses, assess the patient in person, and restart the patient maintaining this dose for at least three consecutive days.

15. The MMT physician shall reduce the dose by 50% or to a dose of 30 mg or less when a patient has missed three or more days during the late stabilization and maintenance phases.
16. The MMT physician shall reduce the dose to 30 mg or less when a patient has missed four or more doses of methadone during the late stabilization and maintenance phases.
17. During the late stabilization phase, when the patient's dose of methadone is still changing, the MMT physician shall see and assess the patient at least once weekly. The MMT physician shall increase the dose by no more than 5-15 mg every 3-5 days, depending on the patient's cravings, opioid use, withdrawal symptoms, and underlying risk for toxicity.
18. The MMT physician shall order an ECG with a corrected QTc interval for patients on doses above 150 mg. and then again after every 30-50 mg. dose increase.

5.1.2 Guidelines

1. During initiation and early stabilization, the MMT physician should avoid prescribing any sedating drugs. The MMT physician should also advise the patient to avoid any new sedating medications/drugs.
2. For patients who are addicted to high daily doses of benzodiazepines the MMT physician should taper either before MMT initiation or small tapering doses should be given during the early stabilization phase, preferably in a supervised setting in consultation with an addiction medicine physician.
3. During the Maintenance Phase, the MMT physician should assess patients weekly to monthly based on the recovery needs of the patient. Patients on contingency management should be assessed more frequently (i.e. weekly). Patients on contingency management with full take-home doses may be assessed less frequently than once a week with long-term abstinence of 6 months of more. MMT physician assessments less frequently than once monthly may occur if the patient is well known to the MMT physician, has been clinically stable and abstinent for a long period of time (i.e. years), and is considered by the MMT physician to be a reliable historian.
4. The MMT physician should identify and manage risk factors for Torsades de Pointes arrhythmias, and should obtain an ECG prior to initiation or during the early stabilization phase for patients with these risk factors. (See Section 4: Initial Patient Assessment, Subsection 4.3.4 Assessment for Torsades de Pointes Risk Factors)
5. The MMT should consider tapering the dose if it is high and if the patient reports sedation or other cognitive effects.
6. When considering assessing a patient for a dose increase, the MMT physician should assess the patient for other conditions that are commonly confused with withdrawal symptoms.
7. If the patient has emesis after taking methadone, the MMT physician should not replace, or if contacted by the dispensing pharmacist should not authorize the replacement of, the dose unless the emesis was witnessed by the MMT physician, or the pharmacist or staff, as the case may be, and it occurred less than 30 minutes after consumption. The replacement dose must be no more than 50% of the regular dose.

5.2 Writing a Methadone Prescription

Safe dispensing of methadone begins with a well-written prescription. All methadone prescriptions should be written on the pads supplied by the Tamper Resistant Prescription Pad Program. Collaboration and communication between the physician and the pharmacist help to enhance patient safety. (See Appendix F: Sample Methadone Prescriptions)

Note: The College intends to develop a standard stamp that can be used as a template for methadone prescriptions.

The prescription shall specify all of the following:

1. Start and end dates
2. Days of week that are to be supervised
3. Take Home doses: number of take-home doses and days of week that are to be given as take-home doses
4. Methadone dose: written in both numbers and words to help to prevent tampering of prescriptions.

Note: It is expected that the daily dose will be mixed in Tang or other crystalline juice to a consistent volume (100 ml is recommended) unless the prescription gives other specific instructions.

5.3 Strategies to Reduce Risk of Overdose

5.3.1 Patient Education

1. Explain to the patient that it takes several weeks to reach the optimal dose of methadone, and it may be dangerous to try to relieve withdrawal symptoms with benzodiazepines, illicit methadone or other drugs. (See Appendix I: Managing Potential Methadone Overdose and Appendix J: Patient Guide on Methadone Overdose)
2. Advise the patient to:

   limit his or her driving or use of machinery after a dose increase, particularly in the first few hours after dosing.

   take the methadone dose in the morning, since the risk of overdose is increased at night (Wolff 2002).
3. Whenever feasible (with the patient's consent), a family member or significant other should be educated about the symptoms of overdose with clear instructions to seek urgent medical help at the first sign of toxicity. A patient information guide may be used for this purpose. (See Appendix J: Patient Guide on Methadone Overdose)

5.3.2 Frequency of visits

The MMT Physician shall assess the patient at least weekly during early stabilization, and shall assess the patient prior to each dose adjustment (i.e. more frequently than weekly if there is more than one dose adjustment per week). However, twice-weekly visits during the first two weeks of treatment are recommended, particularly if the patient is at increased risk for

methadone toxicity. After the initiation and early stabilization stage, patient visits should be scheduled at least every 1-2 weeks.

The physician can schedule an assessment of the patient two to six hours after the methadone dose if there are concerns about sedation with the dose. The physician should inquire about sedation and other side effects.

5.3.3 Take-home doses during initial titration

No take-home doses shall be granted during the first three months of treatment including Sunday take-home doses, holiday carries, pharmacy closure. Accelerated take-home doses after two months treatment may be considered under extraordinary circumstances. (See Section 7: Take-Home Doses, Standard 10 and Subsection 7.4.4 Accelerated Take-Home Schedule). In case of pharmacy closure with no reasonable alternative access to witness dispensing, physicians should consider prescribing 1 weekend take-home dose only after 4 weeks on MMT and 4 consecutive weeks of negative random UDS. (See Section 7: Take-Home Doses, Standard 11 and Subsection 7.4.2 Weekend Take-Home Doses when Weekend Pharmacy Access is Limited)

5.3.4 Sedating Drugs

The MMT physician should avoid initiating prescriptions for sedating drugs during the induction period, and should inquire of the patient as to whether he or she has been prescribed sedating drugs by another physician. If another physician has prescribed the patient sedating drugs, the MMT physician should consult with the other prescriber if the MMT physician has a concern about whether it is appropriate for the patient to continue using the sedating drugs while receiving MMT.

Even moderate, therapeutic doses of sedating drugs may increase the risk of overdose if they are initiated at the same time as methadone and the patient is not fully tolerant to their sedating effects. Patients should also be advised to avoid alcohol, especially during MMT induction.

Only initiate sedating drugs, if indicated, very cautiously during the stabilization phase.

“Sedating drugs” includes benzodiazepines, non-benzodiazepine hypnotics, antipsychotics, antidepressants, dimenhydrinate (Gravol) and other sedating antihistamines.

5.3.5 High-dose Benzodiazepine users

Benzodiazepine abuse and dependence are common in this population. As with opioids, it is difficult to accurately judge a patient’s benzodiazepine use and tolerance, therefore, benzodiazepine tapering, while difficult on its own, can be very complicated and potentially unsafe (due to over sedation) when attempted with methadone initiation. If possible, patients addicted to high doses (50 mg of diazepam equivalent per day) should be tapered prior to methadone initiation. Otherwise, benzodiazepine tapering**,** during the early stabilization phase should be considered, with monitoring in a medically supervised setting. Only small benzodiazepine doses should be used, just enough to prevent severe withdrawal.

5.3.6 Communication with the pharmacist

It is important to have regular verbal communication about the patient's clinical presentation between MMT physicians and pharmacists to enhance patient safety. See Section 15 on Professional Duties and Interprofessional Collaboration.

5.3.7 Intoxication or sedation at the pharmacy

At any stage of MMT, the pharmacist should be instructed to hold the methadone and alert the physician if the patient appears sedated or intoxicated. (See Appendix G: Physician-Pharmacist Treatment Agreement for more information).

5.3.8 Careful assessment prior to dose increases/Clinical Criteria for Dose Adjustment

The physician should consider increasing the dose if the patient has daily cravings, ongoing opioid use, or opioid withdrawal symptoms. Withdrawal symptoms vary between patients. Most patients report a combination of the following

Table 05: Withdrawal Symptoms

Physical Symptoms	Psychological Symptoms
Myalgia	Insomnia
Sweating	Fatigue
Yawning	Anxiety
Rhinitis	Irritability
Nausea	Restlessness

Symptoms usually begin a predictable number of hours after the methadone dose, although there may be some daily variation with the patient's activity level and other factors. With each dose increase, the onset of symptoms is delayed and their severity is lessened. Alternative explanations should be sought if the patient has one isolated symptom (such as insomnia or nausea), or if the patient reports that the onset of symptoms is not related to the time of the dose.

The physician should also enquire about side effects, such as constipation and sedation, as this may affect dosing decisions.

5.3.9 Documentation for Dose Adjustments

At visits where the dose is adjusted, the physician should document:

1. Cluster of withdrawal symptoms
2. Timing of withdrawal symptoms (what time of day they appear)
3. Ongoing drug use and timing of drug use:

   Opioid use at the end of the day may indicate inadequate methadone dose.

   Use of alcohol or benzodiazepines may indicate the need for caution in dose adjustment.

4. Changes in mood and daily activities.

5.4 The Initial Methadone Dose

The physician should base the initial dose on the patient's underlying risk for methadone toxicity. The following factors increase this risk – see Table 04: Patient Factors that Increase Risk of Methadone Toxicity (Albion et al. 2010; Srivastava and Kahan 2006).

Sedating drugs include over-the-counter medication such as Gravol, prescribed medications such as antipsychotics and sedating antidepressants, or drugs of abuse such as ketamine and gamma hydroxybutyrate (GHB). Even therapeutic doses of benzodiazepines can increase risk of methadone toxicity. The MMT physician should look for evidence of benzodiazepine use in the initial drug screen.

Opioid tolerance is difficult to establish by history, so, if in doubt, it is safer to initiate on a lower dose. Lowered tolerance is likely in patients who report non-daily opioid use, daily use of codeine, or daily use of oral opioids at moderate doses. Typically, patients who use opioids intranasally (i.e. snorting) have a lower tolerance than patients who inject opioids. Tolerance is lower in patients who have been abstinent for more than a few days, e.g., patients who have been recently discharged from a correctional facility, withdrawal management centre or treatment centre.

See Table 06: Initial Methadone Dose

Table 06: Initial Methadone Dose

Patient Factors	Initial Dose
Higher risk for methadone toxicity	20 mg or less
Recent abstinence from opioids	10 mg or less
No risk factors or recent abstinence	30 mg or less

5.5 Early Stabilization Phase (0-2 weeks)

Dose increases during the early stabilization phase should take place only after an in-person MMT physician assessment and for patients who are experiencing cravings, ongoing opioid use, and/or a cluster of opioid withdrawals symptoms. MMT physicians should assess patients at least once weekly during this phase. See Table 07: Dosing During Early and Late Stabilization Phase

Table 07: Dosing During Early and Late Stabilization Phase

Patient Factors	Dose Increase	Frequency
Higher risk for methadone toxicity	5-10 mg	Every 3-5 days
Recent abstinence from opioids	5 mg or less	Every 5 days or more
No risk factors or recent abstinence	10-15 mg	Every 3-5 days

5.5.1 Missed Doses during Early Stabilization Phase (0-2 weeks)

During the early stabilization phase, patients should be on the same dose for at least three consecutive days with no missed doses before an increase. The pharmacists should be advised to contact the MMT physician if the patient misses any doses. If two consecutive doses are missed during the early stabilization phase, the pharmacist should be advised to cancel the

prescription until the physician can reassess the patient. Collaborative communication between the physician and pharmacist if the patient misses any doses during early stabilization is essential. The patient must be reassessed in person by the physician and restarted at 30 mg or less.

5.6 Late Stabilization Phase (2-6 Weeks)

Most patients in the late stabilization phase are taking between 50–80 mg of methadone. Most patients during this phase are experiencing only partial relief of withdrawal symptoms, and they often continue to use opioids sporadically.

Dose increases during the late stabilization phase shall be the same as during early stabilization phase until a dose of 80 mg is reached. Dose increases during the late stabilization phase should take place with an in person MMT physician assessment for patients who are experiencing cravings, ongoing opioid use, and/or a cluster of opioid withdrawal symptoms. MMT physicians should assess patients at least once weekly during this phase.

5.6.1 Dosing During Late Stabilization Phase

See Table 07: Dosing During Early and Late Stabilization Phase.

5.6.2 Missed Doses during Late Stabilization Phase

If three or more consecutive doses are missed during the late stabilization phase, the pharmacist should be advised to cancel the prescription until the patient can be reassessed by the MMT physician. The patient must be reassessed in person by the MMT physician. After three consecutive days missed, the dose should be decreased to 50% of the current dose or 30mg. After four or more consecutive days missed, the dose should be decreased to 30 mg or less.

See table 09: Management of Missed Doses.

5.7 Maintenance Phase (6+ Weeks): The Optimal Methadone Dose

The optimal maintenance dose of methadone will relieve withdrawal symptoms, block opioid-induced euphoria and reduce opioid cravings for 24 hours, without causing sedation or other significant side effects. With experience, the MMT physician can reach this dose for the majority of their patients within 2-8 weeks of initiating MMT. The optimal dose range for most MMT patients is 60-120 mg (Bao et al. 2009; Department of Health (England) 2007; WHO 2009). A meta-analysis by Bao et al reported that doses of methadone between 60-120 mg and individualization of doses are associated with better retention in MMT (Bao et al. 2009).

During the maintenance phase (when the dose is 80 mg or more), the MMT physician shall increase the dose by no more than 5-10 mg every 5-7 days.

Dose increases during the maintenance phase should take place with an in person MMT physician assessment and for patients who are experiencing cravings, ongoing opioid use, and/or a cluster of opioid withdrawal symptoms. MMT physicians should assess patients once weekly when ongoing dose adjustments are occurring and less frequently thereafter if required.

5.7.1 Missed Doses during Maintenance Phase

Standards for missed doses during maintenance are the same as those for late stabilization. See section 5.9: Managing Missed Doses and table 09: Management of Missed Doses.

5.7.2 Doses below 60 mg

There is evidence that methadone doses of 60–100 mg are more effective than doses below 60 mg in reducing heroin use and retaining patients in treatment (Bao et al. 2009; Caplehorn and Bell 1991; Faggiano et al. 2003). However, maintenance doses below 60 mg are justified for patients who have no unauthorized opioid use, report no significant withdrawal symptoms or cravings, are at high-risk for methadone toxicity, or are on a tapering protocol.

5.7.3 Doses above 120 mg - Risks of High Methadone Doses

5.7.3.1 Risks of High Methadone Doses

Opioids such as methadone have several side effects that may be dose related, including sedation, overdose leading to death, sleep apnea and sexual dysfunction. High methadone doses are also associated with prolonged QT interval, which can cause

Torsades de Pointes, a ventricular arrhythmia (Abramson et al. 2008; Pimentel and Mayo 2008). One study found that approximately 5% of patients on MMT had QTc > 500 msec, the value associated with increased mortality. All of these patients were on doses in excess of 120 mg (Anchersen et al 2009). Other risk factors for Torsades include, use of cocaine and other stimulants, heavy alcohol consumption, cardiomyopathy, previous MI or valvular abnormalities, a family history of long QT syndrome, liver dysfunction, electrolyte disturbances and medications that affect methadone levels or the QT interval (Abramson et al. 2008; Ehret et al. 2006; Fareed et al. 2010; Justo et al. 2006; Krantz et al. 2009). See table 08: Risk Factors for QTc Prolongation in Patients on Methadone.

Table 08: Risk Factors for QTc Prolongation in Patients on Methadone*

Risk Factor	Examples
Older Age	
Structural heart disease	Myocardial infarction, congestive heart failure, valvular disease, cardiomyopathy
HIV infection	
Low potassium level	On drugs that lower potassium e.g. Diuretics
Low prothrombin level	
On medications that inhibit Cytochrome p450 3A4	HIV antivirals e.g. indinavir Antifungals e.g., Fluconazole, ketoconazole Calcium channel blockers e.g., Diltiazem, verapamil Antimicrobials e.g., Norfloxacin Antidepressants e.g., Fluvoxamine Contraceptives e.g., Mifepristone Foods: e.g., grapefruit juice
Alcohol use	
Cocaine use	
Family or past history of long QT syndrome	History of syncope or sudden cardiac death in the family
On medications that prolong QTc	Cardiac medications e.g., amiodarone, sotalol Antipsychotics e.g., chlorpromazine, haloperidol, pimozide, thioridazine Antibiotics e.g., clarithromycin, erythromycin Anti-nausea drugs e.g., domperidone Tricyclic Antidepressants e.g. amtriptyline, imipramine, etc.

**Adapted from: Methadone – associated QTc prolongation: A case report and review of the literature. (Abramson DW, Quinn DK, Stern TA. Prim Care Comp J Clinic Psychiatric 2008; 10(6): 470-476).*

5.7.3.2 Assessment and Monitoring

High doses of methadone can sometimes have sedating effects that may not be apparent in the physician's office. The MMT physician should inquire about whether the patient or (with the patient's consent) the patient's family has observed cognitive effects such as 'nodding off,' lethargy, diminished concentration or memory.

At baseline, the physician should identify risk factors for torsades, such as heart disease, family history of sudden cardiac death, or concurrent use of medications that affect QT interval (See Table below - Risk Factors for QTc Prolongation in Patients on Methadone). An ECG should be done on patients whose dose is greater than 150 mg (Byrne 2009; Girgis 2009) and repeated for doses of 180-200 mg. Patients with known risk factors for torsades should have an ECG (see Guideline 5.1.2(4)).

5.7.3.3 Management of High Doses

A trial of tapering is indicated for patients who report sedation when on high doses. Clinical experience suggests that tapering to an overall dose decrease of 20-40 mg is tolerated well, and patients often report that they feel more alert and energetic.

The patient should be closely monitored if the QT interval is elevated (> 450 msec for men, > 470 msec for women). Cardiology referral and/or methadone dose reduction should be considered when the QTc exceeds 500 msec, and the MMT physician should take steps to modify risk factors when possible.

5.7.3.4 Ongoing Withdrawal Symptoms in Patients on High Doses

Patients with ongoing withdrawal symptoms despite high methadone doses require ongoing assessment by the MMT physician. Possible causes include:

Rapid metabolism of methadone

Although controversial, peak and trough levels might be useful in patients who continue to report withdrawal symptoms despite doses of 120 mg or higher.

Use of medications that increase the metabolism of methadone

Medications such as Phenytoin, chronic alcohol use.

Continued opioid use

Causes increased tolerance and withdrawal symptoms on opioid cessation.

Dose diversion

The patient consumes some of his/her take-home dose and sells the rest.

Pseudonormalization

After a methadone dose increase, some patients experience very mild mood elevation. They develop tolerance to this effect after a few weeks, prompting them to seek another dose increase.

Insomnia, anxiety, fatigue and other psychiatric symptoms

Because psychiatric symptoms are such a prominent feature of opioid withdrawal, patients may incorrectly attribute these symptoms to withdrawal.

Cocaine use

Cocaine is a methadone inducer (increases the metabolism of methadone) especially when used in large doses. Ongoing use of cocaine may result in the patient complaining of the need for a dose increase. The physician may want to discuss the benefits of abstinence from cocaine.

5.8 Split Doses

Split dosing is commonly used during the management of chronic pain, and occasionally during the management of pregnant patients and patients on medications that induce rapid metabolism of methadone.

5.9 Managing Missed Doses

Missed doses may indicate a variety of problems, including relapse to alcohol or other drug use. Therefore, the physician should reassess the patient's clinical stability. Pharmacists should report missed doses to the MMT physician in a timely fashion. A clinically significant loss of tolerance to opioids may occur within as little as 3 days without methadone; therefore, the MMT physician should reduce the methadone dose in patients who have missed three consecutive days. The dose can be rapidly increased once the response to the lower dose is assessed.

Table 09: Management of Missed Doses

Phase of Treatment	Missed Doses	Action	Dose Change
Early Stabilization (0-2) weeks	1 day missed	No dose increase	• Resume same dose. • Do not increase dose until three consecutive days at the same dose.
	2 consecutive days missed	• Reassess patient in person. • Cancel remainder of prescription	• Restart at initial dose (10-30 mg) for at least 3 days • Reassess after third consecutive dose.
Late Stabilization/ Maintenance	1-2 days missed	• Provide usual prescribed dose if patient is not intoxicated. • Assess patient in 1-2 weeks to determine clinical stability	• No change
Late Stabilization/ Maintenance	3 consecutive days missed	• Reassess patient in person • Cancel remainder of prescription • Reassess every 3-4 days if dose is increased daily	• Restarted at 50% of regular dose or decrease to 30 mg • Then increase dose to no more than 10 mg daily for maximum of 3 days, then reassess by day 3-4. • Thereafter, dose increase of 10-15 mg every 3 -5 days until 80 mg • Then 10 mg every 5-7 days for dose increases above 80 mg
Late Stabilization/ Maintenance	4 or more consecutive days missed	• Reassess patient in person • Cancel remainder of prescription	• Restart at 30 mg or less • Then increase dose no more than 10-15 mg every 3-4 days until 80 mg • Then increase 10 mg every 5-7 days for dose increases above 80 mg.

5.10 Vomited Doses

Vomited methadone doses are not replaced unless a health professional or staff member directly observes emesis. If the emesis was witnessed by the health professional or staff and it occurred less than 30 minutes after consumption, the dose can be replaced at no more than 50% of the regular dose.

Repeated dosing (i.e. replacement) creates a risk of inadvertent overdose. Underlying causes of the vomiting should be addressed. For pregnant patients or patients with underlying medical conditions (e.g. cancer or HIV), the MMT physician may decide to prescribe a replacement dose even if the pharmacy or methadone clinic staff did not observe emesis.

6. Urine Drug Screening (UDS)

Urine Drug Screening (UDS) is one tool to verify patients' self-reported substance use, assess response to MMT and determine suitability for take-home doses.

6.1 Overview

Urine Drug Screening (UDS) is one tool to verify patients' self-reported substance use, assess response to MMT and determine suitability for take-home doses.

Addiction is characterized by periods of abstinence and relapse, and UDS monitoring can assist in detecting periods of relapse and improving effective management. UDS combined with a patient's self-reported drug use are more accurate than either alone (Perrone et al. 2001; Ries et al. 2002). Providing take-home doses to methadone patients with drug-free UDS is an effective strategy for reducing opioid and other drug use (contingency management) (Chutuape et al. 1996 a & b; Iguchi et al. 1988; Preston et al. 2002; Schmitz et al. 1998; Stitzer et al. 1992).

6.1.1 Standards

1. The MMT physician shall obtain and interpret UDS tests for routine screening of opioids (including methadone), cocaine, amphetamines and benzodiazepines for the purpose of monitoring and managing the patient.
2. The MMT physician shall obtain and interpret a UDS prior to MMT initiation.
3. The MMT physician shall obtain and interpret weekly UDS for 4 weeks prior to and for 4 weeks following acquisition of take-home doses (See Standards, Section 7: Take-Home Doses).

6.1.2 Guidelines

1. The MMT physician should consider chromatography testing (if available) if the patient uses substances that are difficult to detect with immunoassays (e.g., fentanyl, amphetamines), if the patient disputes the test results, or if there is an unexpected result and the patient faces serious consequences for a positive test (e.g., loss of take-home doses, child custody).
2. The MMT physician should monitor the UDS collection to minimize the risk of receiving a tampered urine sample. The MMT physician should use strategies such as:
   a) witnessed collection or supervised collection,
   b) checking the bathroom before the patient goes in for bags or extraneous items,
   c) requiring the patient to remove bulky clothing and boots, and
   d) temperature monitoring, measurement of pH, creatinine, or specific gravity.

   Note: This Standard applies to the administration of UDS in the MMT physician's office or clinic. Where UDS is administered by a laboratory or in a hospital setting, it is expected that the laboratory or the hospital will have established its own UDS standards and guidelines. If a sample taken in an MMT physician's office is to be tested at an off-site laboratory, the sample should be delivered by a secure courier (and not by the patient or by anyone else on behalf of the patient).
3. The MMT physician should conduct UDS on a random schedule. If a random schedule is not possible, then a fixed schedule should be conducted on a weekly basis.

4. The MMT physician should consider the variables involved in UDS interpretation, such as detection times, drug thresholds, false positives, false negatives, and measuring active metabolites (See Appendix P: Urine Drug Test Interpretation).
5. The physician's response to positive UDS should be non-punitive, and should assist the development of a treatment plan that promotes patient recovery.
6. The MMT physician should order UDS at a minimum of once monthly for all patients on methadone maintenance.
7. The MMT physician should take into consideration treatment benefits, as well as the effect on treatment retention, and cost where weekly (rather than monthly or bi-weekly) UDS is used during the maintenance phase.
8. Providing a tampered urine sample or failure to attend for a requested UDS within 24 hours (48 hours in occasional exceptional circumstances) should be handled in the same fashion as if the UDS is positive.

6.2 UDS Techniques

There are two methods for UDS, immunoassay and gas chromatography/mass spectrometry. Immunoassay is rapid, practical and inexpensive. It can be performed in the laboratory or point-of-care (dipstick). Immunoassay uses a labeled antigen, which competes with the drug being tested to bind with an antibody. The amount of labeled antigen-antibody is inversely proportional to the drug present. Immunoassay generally detects drug classes (usually morphine for opioids and diazepam for benzodiazepines). This results in lower specificity for opioid screening. Synthetic opioids (meperidine, fentanyl and methadone) are not detected and semi-synthetic opioids (oxycodone and hydromorphine) are only sometimes detected. Opioid-specific immunoassay tests can be obtained for these opioids.

Immunoassay tests can produce false positive results due to cross-reactants, particularly with amphetamines.

Gas chromatography/mass spectrometry separates specimens into component molecules, and identifies and measures unique structural features. It detects specific drugs with high sensitivity (99%) and specificity (99%). It is more expensive and time-consuming, and is generally used to confirm an unexpected result from immunoassay or a result that may have significant consequences for the patient (e.g., loss of take-home doses, notification of child services).

6.3 Urine Tampering/Substitution

Urine tampering can occur through dilution, ingestion of certain drugs (i.e., diuretics, sodium bicarbonate, salicylates), adulteration of the urine (i.e, drain cleaner, bleach, soap, ammonia, lemon juice, hydrogen peroxide) and urine substitution. The validity of a urine sample should be ensured by either directly witnessing the collection of urine or by supervising the collection using the techniques in Table 10: Methods of Tampering and Monitoring Process.

See Table 10: Methods of Tampering and Monitoring Process. (next page)

TABLE 10: METHODS OF TAMPERING AND MONITORING PROCESS

Methods of Tampering	Safeguards
Through dilution, ingestion of certain drugs such as: • Diuretics • Sodium bicarbonate • Salicylates **Adulteration of the urine with:** • Drain cleaner • Bleach • Soap • Ammonia • Lemon juice • Hydrogen peroxide • Urine substitution	• Not wearing heavy clothing • A temperature strip on the container • The measurement of pH (4.5 to 8) • Specific gravity (1.002 to 1.020) • Urine creatinine (< 2 to 3 mmol/liter non-physiologic) • Pre-labeled containers • Turn off hot water

6.3.1 Method of Collection

Urine for drug screens should be collected in the office (either witnessed or supervised) and at random intervals. This should be the standard, but if this is not possible, urine drug screens can be collected at a community laboratory. The patient's identity must be confirmed at the time of urine collection. The following safeguards may be taken to minimize the risk of urine tampering:

Clothing

Patients must divest themselves of coats, jackets, other bulky clothing and bags, all of which must be left outside the bathroom.

Sample Temperature

Hot water may be turned off in the bathroom. Patients should be provided with a pre-labeled container and a staff member should record the temperature of the urine sample immediately. Other monitoring measures as above are encouraged.

Witnessed Collection

It is usually sufficient that urine be collected in a supervised fashion according to the standards listed above, but, witnessed urine collection may occasionally be deemed necessary to ensure the authenticity of the sample. In these cases, patients should provide the urine sample while in the presence of an appropriate methadone clinic staff member.

6.4 UDS Interpretation and Response

The process of interpreting UDS results requires consideration of detection times, test thresholds, metabolites being measured and circumstances that cause false positive and negate negative results.

False positive results can occur when a cross reactant produces a positive result with immunoassay testing. This is particularly common with amphetamines, but can occur with other substances (See Appendix P: Urine Drug Test Interpretation). False positive results can occur when a consumed opioid metabolizes into another opioid (morphine is a metabolite of codeine and hydromorphone is a metabolite of morphine), and the metabolite is detected. False negative results occur when a synthetic or semi-synthetic opioid and/or certain benzodiazepines (clonazepam and lorazepam) are present, but not detected due to the limitation of drug class detection with immunoassay or when a substance is present, but at a level which is below the cut-off value.

The response to UDS results should be non-punitive. A positive test can assist in developing a treatment plan with the patient. Patient management combined with counseling and support is essential in helping patients quickly recover from a relapse and in preventing it from becoming sustained.

The MMT physician should ensure that the benefit from increasing frequency of required urine drug screening be balanced with potential negative consequences on the patient's work and family obligations.

6.5 Initial UDS

Initial UDS results should confirm the presence of opioids and, ideally, identify the patient's primary opioid of abuse. Either an opioid-class or an opioid-specific immunoassay may be used. If an opioid-class immunoassay is used and fails to identify a patient's specific opioid or current opioid use, it may be sufficient to initiate a patient on methadone if there is strong clinical evidence that the patient is opioid-dependent, as defined by the following conditions:

1. The patient has signs and symptoms of obvious opioid withdrawal
2. The patient has obvious track marks
3. The patient has been on previous MMT and is at imminent risk of relapse
4. The patient has been dependent in the past and is at imminent risk of relapsing (e.g., recent release from incarceration)

The MMT physician should:

1. Obtain corroborating information from a previous opioid prescribing physician and/or reliable agencies.
2. Consider a consultation with an experienced methadone maintenance prescriber.
3. If the initial UDS is inconsistent with the patient's reported opioid use (e.g., the patient reports daily oxycodone use and the oxycodone is negative in the UDS), the MMT physician should address this inconsistency with the patient and conduct a more thorough assessment to confirm a diagnosis of opioid dependency prior to initiating MMT.

6.6 UDS Collection Schedule

UDS should be obtained 1 to 4 times a month during the induction, stabilization, and maintenance phases. A random collection schedule is preferred over a fixed schedule (UDS obtained at patient visits) to minimize the possibility of patients avoiding drug use detection by timing their use according to the UDS schedule. If a fixed schedule is used, then weekly urines on variable days is encouraged.

More frequent UDS (more than once a month) is more likely to detect sporadic drug use, and in some patients may facilitate more accurate self-disclosure and better patient management.

When determining a UDS schedule, the MMT physician should consider the balance between the potential benefits of more frequent UDS and the potential risks – including interference with the patient's work or family obligations and the costs of the test. When a patient is notified of urine drug screen requirement, they should normally be expected to provide the sample within 24 hours (48 hours in occasional exceptional circumstances).

If the patient demonstrates signs suggestive of relapse, the MMT physician should increase the frequency of UDS to weekly for as long as the signs are present.

6.6.1 UDS Collection Schedule with Take-Home Doses

Take-home doses are an essential component of long-term success for patients during the maintenance phase. If take-home doses are being considered, more frequent UDS are initially required to confirm abstinence from drug use, which could increase the risk of diversion or irresponsible handling of take-home methadone doses.

Prior to acquisition of take-home doses, four consecutive weeks of documented negative random UDS tests should be obtained. Weekly UDS should be obtained for a minimum of 4 weeks after take-home doses has been initiated. The frequency of UDS may then decrease to twice a month for two months, and thereafter to once monthly depending on the clinical situation.

If the patient has a positive UDS, the take-home doses should be discontinued (see Section 7.7 Take-Home Doses for Patients on Benzodiazepines or Opioids). The loss of take-home doses in response to a positive UDS is not done to punish the patient, but rather to reduce the risk of methadone diversion in the community.

The MMT physician should ensure that the benefit from increasing frequency of required urine drug screening be balanced with potential negative consequences on the patient's work and family.

7. Take-Home Doses

Take-home doses are key to the success of MMT.

7.1 Overview

Take-home doses are key to the success of MMT. Controlled trials have demonstrated that MMT patients markedly reduce their use of heroin and cocaine when given take-home doses contingent upon drug-free UDS (Chutuape et al. 1996 a & b; Iguchi et al. 1988; Preston et al. 2002; Schmitz et al. 1998; Stitzer et al. 1992).

There is strong evidence that methadone take-home doses contingent on drug-free UDS prevent the decline in treatment outcomes over time, and are an effective strategy for reducing opioid and other drug use (contingency management) (Chutuape et al. 1996 a & b; Iguchi et al. 1988; Preston et al. 2002; Schmitz et al. 1998; Stitzer et al. 1992). Surveys and observational studies have found that patients strongly value take-home doses, and treatment retention rates are lower in clinics with restrictive take-home policies (Amass et al. 1996; Amass et al. 2001; Pani et al. 1996).

7.1.1 Standards

1. When prescribing take-home doses, the MMT physician shall ensure that patients understand how to store their methadone securely, that they understand the risks of diverted methadone, and that they agree never to give or sell their dose to others.
2. The MMT physician shall not prescribe take-home doses before 3 months in the MMT program (See Standards 10, 11 and 12, of Section 7 Take-Home Doses for unique exceptions)
3. The patient must sign a written take-home dose agreement (Appendix L: Take-Home Dose Agreement).
4. The MMT physician shall not prescribe take-home doses to patients who refuse consent to the MMT physician communicating with their opioid or benzodiazepine prescriber.
5. The MMT physician shall prescribe a maximum of six take-home doses per week. The daily dose to be mixed in Tang or other crystalline juice to a consistent volume (100 ml is recommended).
6. On the day the MMT patient picks up their take-home doses, the ingestion of dose for that day must be witnessed.
7. The MMT physician shall not prescribe take-home doses if:
    a. The patient has an unstable or untreated mental illness (including active addiction) or cognitive impairment
    b. The patient continues to use drugs, including alcohol in a risky fashion, cocaine, amphetamines, or opioids or benzodiazepines unless prescribed by another physician (see Section 7.7 Take Home Doses for Patients on Benzodiazepines or Opioids)
    c. The patient is not able to safely store the methadone (See Subsection 7.2.2 Locked Box)
    d. There is reasonable evidence that the patient is diverting or suspected of diverting methadone

    e. The patient does not understand the risks of methadone diversion, such as in the case of cognitive impairment
8. The MMT physician shall discontinue all take-home doses immediately if the patient has a relapse to substance use, or in the following situations:
    a. There is reasonably strong evidence that the patient has diverted their methadone dose, or has tampered with their UDS.
    b. The patient has missed three or more days of methadone (except in unavoidable circumstances such as hospitalization).
    c. The patient has become homeless or has unstable housing, and can no longer safely store their methadone.
    d. The patient is actively suicidal, cognitively impaired, psychotic, or is otherwise at high risk for misuse of their methadone dose.
    e. The patient has recently been released from jail when incarcerated for prolonged periods of greater than 3 months.
9. The daily observed dose shall be reduced if the MMT physician suspects the patient may not have been taking or may not be tolerant to the full take-home dose.
10. The MMT physician shall only prescribe an accelerated take-home schedule after 2 months if:
    a. There is good reason to believe that prolonged daily dispensing is likely to cause the patient to drop out of treatment AND
    b. None of the conditions listed in Standard 7, Section 7 Take-Home Doses is present
11. The physician shall only prescribe a weekend take-home dose after 4 weeks in MMT if the patient (all conditions shall be met):
    a. Lives in a community that does not have a pharmacy that is open on a weekend day (for example Sunday)
    b. Has no hospital available for weekend dispensing
    c. Has had 4 consecutive weeks of random negative UDS
    d. Does not have transportation to a pharmacy in a different community
    e. None of the conditions listed in Standard 7, Section 7 Take-Home Doses is present
12. The MMT physician shall only prescribe take-home doses that are exceptions to the take-home dose schedule if: (See Section 7.4 Take-Home Doses in Exceptional Circumstances)
    a. The patient is able to safely store the medication and has good insight for take-home dose safety issues
    b. The patient is emotionally stable and displays good judgment to recognize the risks for methadone misuse or diversion
    c. None of the conditions listed in Standard 7, Section 7 Take-Home Doses is present
13. The MMT physician shall not reinstate take-home dose within the first month for a patient who has been recently released from jail (See Section 7.6.2 Suspending Take-Home Doses for Reasons Other than Substance Use).
14. The MMT physician shall suspend take-home doses for patients who consume them early, or who report lost or stolen take-home doses even on one occasion.
15. Patients wishing to receive take-home doses shall have random weekly UDS that are negative for four consecutive weeks prior to obtaining take-home doses. After take-home doses have been initiated, random UDS shall be obtained weekly for a minimum of four weeks and then every two weeks for a minimum of eight weeks. The frequency of random UDS may then decrease to once monthly according to individual clinical and social circumstances.

16. For patients on take-home doses, the MMT physician shall consider increasing the frequency of UDS (weekly) if the patient is suspected of lapse or relapse. The frequency shall be reduced accordingly based on the response of the patient.
17. Long-term benzodiazepine use is generally inappropriate and potentially dangerous in MMT patients. Patients will not be eligible for take-home doses while on benzodiazepines unless there are exceptional circumstances as outlined in the text (See Standard 4 and Guideline 13 of Section 7 Take-Home Doses and Section 7.7 Take-Home Doses for Patients on Benzodiazepines or Opioids).
18. If a patient receiving take-home doses has a positive UDS or discloses drug use, take-home doses will be discontinued immediately and the patient's clinical stability shall be reassessed.

7.1.2 Guidelines

1. Prior to prescribing the first take-home dose, the MMT physician should instruct the patient to show a locked box that will be used for the safe storage of take-home doses.
2. Under Standard 7.1.1(2), the MMT physician shall not prescribe take-home doses until the patient has been in the program for 3 months, and prior to take-home dose acquisition the patient has had at least 8 weeks without substance use, as determined by history and UDS. The MMT physician should prescribe additional take-home doses by one of the two following protocols:
    a. **Schedule A**: Starting with one take-home dose per week increasing at a rate of no more than one take-home dose per week every four weeks, to a maximum of six take-home doses. Each additional take-home dose should be prescribed only after the patient has had at least four additional weeks without substance use.
    b. **Schedule B**: Starting with two daily take-home doses on consecutive weekend days. After a further eight weeks free of substance use, take-home doses are increased to one carry of three consecutive days and one carry of two consecutive days with intervening witnessed dose. After an additional 12 weeks free of substance use take-home doses can be increased to six take-home doses a week.
3. In the accelerated schedule (per Section 7, Standard 10), the MMT physician may prescribe the first take-home dose after 2 months on MMT, with at least 4 consecutive weeks of negative UDS, and subsequent increase in take-home dose at a rate of no more than one extra take-home dose per week, every two to four weeks, to a maximum of six take-home doses per week.
4. Take-home doses should not be prescribed to accommodate pharmacy closures. The MMT physician should prescribe the weekend dose at an alternate pharmacy if the patient's regular pharmacy is closed on a weekend day. The MMT physician should contact the two pharmacies to ensure they are aware so that they can coordinate confirmation of no missed doses using receipts or other methods.
5. MMT physicians working in communities without a pharmacy open 7 days per week should consider negotiating with the local hospital (if it dispenses methadone) to provide weekend dispensing, or arranging for the methadone to be dispensed at the nearest hospital.
6. The MMT physician may prescribe exceptional take-home doses on compassionate grounds for patients who have a personal or family crisis and are not yet receiving take-home doses. The patient should be clinically stable and low-risk as measured by self-report, UDS and social indicators, and should have been on MMT for at least 2 months. A maximum of six take-home

doses should be given at a time. The MMT physician may give exceptional take-home doses for well documented and sound personal reasons or holidays for patients who have been on MMT for at least two months and have had at least four weeks of negative UDS, and are approaching a stable methadone dose, and are receiving one to two take-home doses per week. A maximum of six take-home doses should be given at a time. The MMT physician should ensure that the previous take-home dose level is resumed after the period of exceptional take-home dose.

7. If a local pharmacy cannot be found to dispense methadone, the MMT physician may give exceptional take-home doses for work or vacation travel for patients who are clinically stable, have not had drug use for 12 months and are receiving 3 to 6 take-home doses per week. A 13-day dose is the maximum that may be given at a time in special situations. The MMT physician should request documentation of travel plans. The MMT physician should ensure that the previous take-home dose level is resumed after the period of exceptional take-home dose. (See Section 7.8 Routine 13-Day Take-Home Doses for Work Commitments).
8. During a relapse for any drug use, the MMT physician should immediately suspend all take-home doses until re-stabilization has been demonstrated via negative UDS for at least 1 month, and then reinstate at a rate of one take-home dose per week to one take-home dose per month depending on the reliability of the patient and demonstrated abstinence.
9. During a relapse of greater than one month, the MMT physician should suspend all take-home doses until re-stabilization has been demonstrated via negative UDS for at least two months. Take-home doses may then be reinstated at the regular rate using one of the protocols in Guideline 2, Section 7 Take-Home Doses contingent on negative UDS and no reported drug use.
10. The MMT physician may reinstate take-home doses after 1 month for patients who remain clinically stable without drug use, and:
    a. Had take-home doses cancelled due only to missed doses
    b. Has been incarcerated for less than 3 months
11. For patients who have tampered with their UDS in an attempt to conceal a relapse or failed to provide a sample in a timely manner, the MMT physician may reinstate take-home doses after a one-month period at a rate of one take-home dose per week to one take-home dose per month depending on the patient's reliability and clinical stabil
12. The MMT physician may decide to restrict take-home doses indefinitely if there has been proven or suspected diversion. A second opinion with another MMT physician should be considered before reinstituting the take-home dose.
13. The MMT physician should be very cautious about prescribing take-home doses to clinically stable patients who are being prescribed benzodiazepines or opioids. This is generally not recommended. The MMT physician may provide take-home doses in this population only under very specific circumstances as outlined in Section 7.7 Take-Home Doses for Patients on Benzodiazepines or Opioids.
14. The prescribing of exceptional take-home doses under Guideline 7.1.2(6) or 7.1.2(13) should be documented and communicated to the dispensing pharmacist.

7.2 Take-Home Doses: Risks

7.2.1 Diversion

To reduce the risk of diversion and the associated societal harms, the ingestion of the MMT patient's methadone dose for the day the patient picks up his/her take-home doses must be witnessed.

Regularly ensuring that the patient is able to tolerate their dose of methadone also eliminates the risk of overdose that could occur if a patient had not actually been taking their full methadone dose and were abruptly expected to take their full methadone dose (such as upon hospitalization or incarceration) in a daily witnessed fashion. This requirement is in line with well-established best practices in the field of addiction medicine, and is included in essentially every provincial MMT guideline in Canada.

Diversion of take-home doses is a serious public health problem. The use of methadone for analgesia has increased sharply in the US, with a 7-fold rise from 1997 to 2004. This has been accompanied by a 17-fold increase in methadone-related deaths (Sims et al. 2007).

The risk of diversion and accidental or intentional misuse increases in patients who:

1. Have suicidal ideation or cognitive impairment **OR**
2. Are homeless, living in a shelter or transiently housed **OR**
3. Are actively addicted to alcohol, cocaine, benzodiazepines or other drugs

The last group is at higher risk because they may sell their methadone in order to pay for their drug use, and are at greater risk for overdose due to interactions between methadone and the abused drug.

7.2.2 Locked Box

To increase the safety of storing methadone at home, patients can be asked to use locked boxes (Breslin et al. 2006).

Before take-home doses are prescribed, the physician should ask patients to bring in a locked box to demonstrate that they are able to store methadone safely. This is particularly important for patients who have children, adolescents or young adults living at home. *Newfoundland and Labrador Pharmacy Board Standards of Pharmacy Practice – Methadone Maintenance Program* requires that pharmacies collaborate and cooperate with physicians in providing consistent messaging and procedures with respect to locked boxes.

The standards recommend that the locked box be used to store the take-home doses in the refrigerator to ensure that there is no opportunity for accidental or intentional ingestion of methadone by individuals who are naïve to methadone.

7.3 Take-Home Doses: Criteria

Take-home doses are an essential component of long-term success for patients during the maintenance phase.

The criteria for determining appropriateness for take-home doses are based on patient and community safety, and on clinical stability, where clinical stability can be defined by:

1. Stable dose of methadone (with allowances for occasional dose increases or when tapering)
2. No recent drug or alcohol use
3. Compliance with treatment directives
4. Stable housing
5. Emotional stability and good insight into take-home dose safety issues
6. Capability to be reached in a timely fashion for notification of requirement for UDS (typically being accessible by telephone)

Collaborative communication with the pharmacist will facilitate and provide information about the patient's daily clinical presentation and stability.

Prior to prescribing take-home doses, the physician should carefully explain the risks of methadone diversion or misuse, lethality and the patient's responsibility to store and use their dose safely.

It must be stressed to the patient that the average daily dose of methadone may result in death if taken by a person not dependent on an opioid. Single dose overdose cases resulting in death have been reported with methadone doses as low as 40 mg in non-tolerant patients (Source: CPSNS Methadone Maintenance Treatment Handbook)

If take-home doses are being considered, more frequent UDS are required initially to confirm abstinence from drug use which could increase the risk of diversion of or irresponsible handling of take-home methadone doses.

Prior to acquisition of take-home doses, four consecutive weeks of documented negative random UDS tests should be obtained. After acquisition of take-home doses, random negative UDS should be obtained weekly for a minimum of four weeks and then every two weeks for a minimum of eight weeks. The frequency of UDS may then decrease to once a month depending on the clinical situation.

A written take-home dose agreement must be signed by the patient (See Appendix L: Take-Home Dose Agreement).

7.4 Take-Home Dose Acquisition Schedules

7.4.1 First Take-Home Dose

Patients are eligible for their first take-home dose if they meet the criteria for clinical stability and prior to take-home dose acquisition the patient has had at least 3 months in MMT and 2 months without substance use, as determined by history and UDS.

7.4.2 Weekend Take-Home Doses when Weekend Pharmacy Access is Limited

Some communities do not have a pharmacy that is open on weekend days, forcing patients to travel to a pharmacy in a different community. This can be disruptive and costly, and it may cause some patients to drop out of treatment. Yet, any take-home dose in the first few weeks of MMT can be hazardous; unstable patients may take the extra take-home dose early, putting them at high risk for toxicity.

In an attempt to promote treatment retention while reducing the risk of toxicity, the guideline allows for a weekend take-home dose after only 4 weeks of negative UDS for patients who do not have access to a pharmacy on a weekend day.

For patients with no take-home doses, if the patient's regular pharmacy is closed on a weekend day (such as Sunday), an alternate pharmacy should be used. The physician should collaboratively communicate with both pharmacies to coordinate shared dosing including that the pharmacies confirm the patient has not missed the previous dose at the other pharmacy.

MMT physicians who work in communities without a weekend pharmacy are encouraged to arrange weekend dispensing with their local hospital (if it dispenses methadone).

7.4.3 Subsequent Take-Home Dose Acquisition

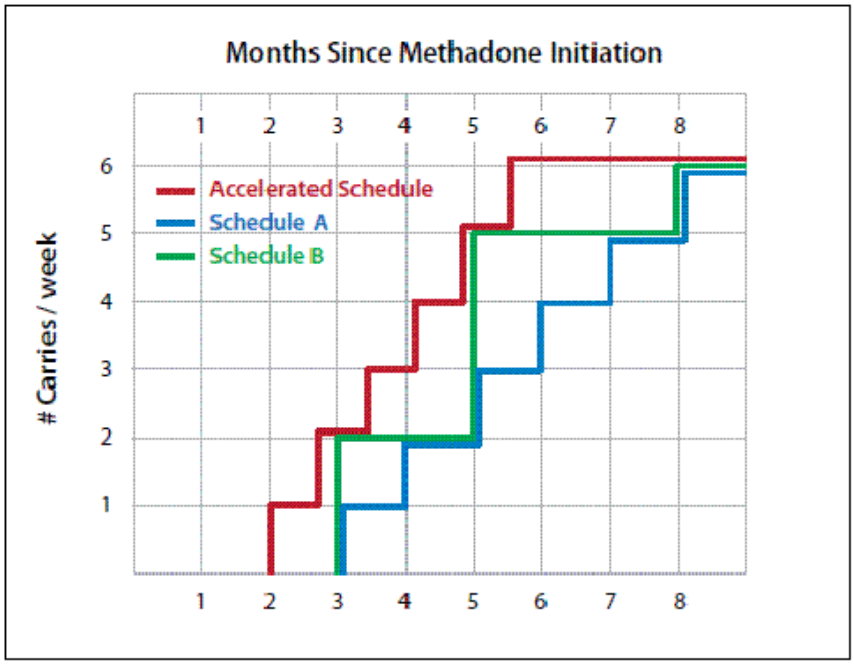
Subsequent increases in take-home doses occur no more often than every 4 weeks with evidence of clinical stability according to **one** of the following schedules:

Schedule A: Starting with one take-home dose/week increasing at a rate of no more than one take-home dose per week every 4 weeks, to a maximum of six take-home doses per week. Each additional take-home dose should be prescribed only after the patient has had at least 4 additional weeks without substance use, **OR**

Schedule B: Starting with two daily take-home doses on consecutive weekend days. After a further eight weeks free of substance use take-home doses are increased to one carry of three consecutive days and one carry of two consecutive days with intervening witness. After an additional 12 weeks free of substance use take-home doses can be increased to six take-home doses a week.

Occasional dose adjustment/increases may occur during take-home dose acquisition provided the patient is clinically stable.

TAKE-HOME DOSE ACQUISITION SCHEDULE



7.4.4 Accelerated Take-Home Schedule

Patients who have regular work, full-time educational programs or family commitments may find it difficult to attend the pharmacy daily, causing them to drop out of MMT. These patients may receive take-home doses at an accelerated rate if they are at lower risk for misuse of their take-home doses, (i.e., they are clinically stable, are not currently addicted to other substances and do not have active mental illness). The first accelerated take-home dose may be given after two months, with one additional weekly dose every two to four weeks. Patients should have at least four consecutive weeks free of substance use before receiving their first take-home dose and then continue to have negative UDS as they increase the number of take-home doses. Only a minority of MMT patients will likely require accelerated take-home doses.

7.5 Take-Home Doses in Exceptional Circumstances

MMT patients sometimes request take-home doses due to family crisis or vacation. Alternative arrangements to dispense daily methadone at a pharmacy in another community, or arrangements for another methadone prescriber to see the patient in another community should be exhausted before allowing exceptional take-home doses.

Before prescribing take-home doses for exceptional circumstances, the MMT physician should attempt to verify the patient's personal or family crisis (with corroborating information from a third party, which should only be sought with the knowledge and consent of the patient; if the patient will not consent, the physician should not accept that there are exceptional circumstances) or travel plans, particularly if the MMT physician doesn't know the patient well or is unsure about the patient's reliability. The MMT physician may choose to communicate with the pharmacist to get corroborating information regarding recent patient stability in preparation for "exceptional take-home dose." The

previous take-home dose level should be resumed after the period of "special take-home dose." See Table 11: Criteria for Prescribing Exceptional Take-Home Doses to review the suggested criteria for prescribing exceptional take-home doses.

In a situation where the patient is clinically stable, and receiving 3 to 6 take-home doses per week, exceptional take-home doses may be given in the case of travel for work or vacation, but only if a local pharmacy cannot be found. The patient should provide documentation of travel plans. A 13-day dose is the maximum that may be given at a time in such special situations. The previous take-home dose level should be resumed after the period of exceptional take-home dose.

Table 11: Criteria for Prescribing Exceptional Take-Home Doses

IF:	THEN:
The Patient has been on MMT for at least two months and is not yet eligible for any take-home doses, but is stable and is not considered high-risk for diversion	• Give take-home doses on compassionate grounds only, e.g., a personal crisis • Give no more than six take-home doses at a time.
The patient has been on MMT for at least 2 months and has negative random UDS for at least 4 weeks, is approaching a stable methadone dose.	• Give take-home doses for sound personal reasons only e.g., vacation / holidays, family matters. • Give no more than six take-home doses.
The patient has not had drug use for 12 months, is clinically stable and receiving 3- 6 take-home doses per week.	• Give up to 13 day take-home doses for travel purposes. • If more than 13 days of take-home doses is required, a second opinion with another MMT physician is suggested.

7.6 Suspending Take-Home Doses

7.6.1 Relapse to Drug Use

Take-home doses should be discontinued if patients have had ANY relapse to drug use (including non-prescribed opioids, cocaine, amphetamines, benzodiazepines, and alcohol in a risky fashion).

If the patient has tampered with their UDS or failed to provide a urine sample in a timely manner in an attempt to conceal a relapse, the physician should respond in the same manner as to a relapse to drug use, and cancel take-home doses immediately.

Take-home doses should not be reinstated until stability can be re-established objectively via weekly UDS and other measures of clinical stability.

In patients whose drug use was sporadic and brief, and whose clinical stability is not significantly compromised, take-home doses may be resumed after 1 month – in a step-wise fashion up to the previously scheduled rate depending on the reliability of the patient – and demonstrated abstinence.

In patients who have had a longer relapse with loss of clinical stability, take-home doses may be resumed after at least 2 months of stability and introduced at the same rate as patients newly acquiring take-home doses.

Increased counseling and supportive care may help the patient recover from a relapse before it causes serious physical or social damage. The frequency of UDS should be increased to weekly, the intensity of counseling and follow-up should be increased, and take-home doses should be reinstated at a gradual rate when the relapse has resolved.

7.6.2 Suspending Take-Home Doses for Reasons Other than Substance Use

The MMT physician should strongly consider suspending take-home doses if the patient consumes take-home doses early, or reports lost or stolen take-home doses even one time. Some patients, especially those with mental health issues or addiction recovery needs, may benefit from increased structure of observed dosing at the pharmacy, and therefore decreased take-home doses.

Patients for whom there is strong evidence of diversion should have their take-home doses restricted indefinitely, as there is no reliable method to prevent diversion if their take-home doses are reinstated.

A second opinion with another MMT physician should be sought prior to reintroduction of the take-home doses, where appropriate and feasible.

Take-home doses should also be cancelled in patients who no longer have stable housing, have missed 3 or more days of methadone (except in unavoidable circumstances), or have a mental illness that places them at high risk for misuse of take-home doses. Because patients who have been incarcerated for prolonged periods are often clinically unstable on release, they should have daily witnessed ingestion of methadone in the first month after discharge from jail even if they had take-home doses prior to their incarceration. Once clinical stability has been re-established, the take-home doses may be reinstated at rate consistent with “Schedule A” or “Schedule B” in Guideline 2, Section 7 Take-Home Doses.

In certain circumstances, take-home doses may be reinstated at the previous level after 1 month of daily witnessed ingestion if the doses were abruptly cancelled because the patient missed 3 or more doses, or because the patient was incarcerated. In either case, the take-home doses should only be reinstated if the patient remains clinically stable and is not using drugs.

7.7 Take-Home Doses for Patients on Benzodiazepines or Opioids

The prescribing of benzodiazepines for long-term use is generally inappropriate.

The MMT physician should be very cautious about initiating or continuing a prescription for take-home doses of methadone for patients while they are on benzodiazepines or opioids unless they are clinically stable and there are exceptional circumstances and the other conditions identified below are met.

Exceptional circumstances will include:

i. where benzodiazepines are prescribed or recommended by a treating psychiatrist or neurologist; or
ii. where opioids are prescribed or recommended by a treating physician for the short term treatment of acute pain; or
iii. where opioids are prescribed or recommended by a pain specialist for chronic pain or
iv. other circumstances analogous to (i), (ii), and (iii) where benzodiazepines or opioids have been prescribed by a treating physician.

Where the above circumstances exist, the MMT physician should consult with the opioid or benzodiazepine prescriber, and should be satisfied that the benefit to the patient outweighs the risk of use of the benzodiazepine or opioid concurrently with MMT.

Where benzodiazepines or opioids are being prescribed concurrently with methadone there should be controlled dispensing, usually in a similar fashion to their methadone dispensing.

MMT physicians may communicate with other prescribers within the patient's circle of care based on implied consent. If the patient has expressly indicated that he or she does not wish for the MMT physician to contact the patient's opioid or benzodiazepine prescriber, MMT physicians should not prescribe take-home doses. The MMT physician may, however, contact the opioid or benzodiazepine prescriber despite this refusal if the physician reasonably believes that it is necessary to prevent or reduce a risk of serious harm to the health or safety of the patient or someone else, or is necessary for public health or public safety.

The MMT physician should only provide take-home doses of methadone to patients who are concurrently being prescribed benzodiazepines or opioids if all of the following conditions are met:

- The patient has a medical or psychiatric diagnosis that is currently stable and warrants the use of the benzodiazepine or opioid under one of the exceptional circumstances outlined above;
- The patient is on a low to moderate therapeutic dose of the benzodiazepine or opioid;
- The patient has not shown signs of benzodiazepine or opioid misuse or toxicity;
- The patient has not expressly refused to allow the MMT physician to discuss their management with their opioid or benzodiazepine prescriber.
- The patient is prescribed and dispensed the medications with controlled dispensing, usually in a similar fashion to their methadone dispensing; and
- The patient meets all other criteria for take-home dose eligibility set out in Section 7 of these Standards and Guidelines.

Regardless of the level of take-home doses, the MMT physician should periodically attempt to taper the benzodiazepine or opioid, particularly if the dose is high (daily equivalent of diazepam 50 mg per day, or morphine 200 mg per day). See Section 10, Subsection 10.4 Benzodiazepines.

The MMT physician should also consider the tapering of methadone if there is a strong possibility that the patient is misusing the medications or is on an unsafe combination.

7.8 Routine 13-Day Take-Home Doses for Work Commitments

In exceptional circumstances, some patients who are on six take-home doses, who have work schedules that make it difficult to go to the pharmacy for weekly dispensing may benefit from extended 13-day take-home doses.

The following criteria must be met to regularly prescribe 13-day take-home on doses:

1. While on MMT, they have a documented history of full take-home doses and clinical stability (no positive UDS) for the preceding 5 years or more **AND**
2. There have been no past reported mishaps with lost or stolen carries **AND**
3. They are working, in school or have daily family commitments that make weekly attendance at a pharmacy difficult **AND**
4. The methadone dose is 120 mg or less

These patients may be prescribed a maximum of 13 take-home doses with one witnessed ingestion prior to each dispensing.

8. Voluntary and Involuntary Withdrawal from MMT

Withdrawal from MMT is most likely to be successful if the patient has been abstinent from illicit substances for a substantial period of time, does not have current or untreated psychiatric co-morbidity, has strong and social supports and is engaging in counseling. (Magura and Rosenblum, 2001)

8.1 Overview

Withdrawal from MMT is most likely to be successful if the patient has been abstinent from illicit substances for a substantial period, does not have current or untreated psychiatric co-morbidity, has strong social supports and is engaging in counseling. (Magura and Rosenblum, 2001). Ideally, the period of abstinence from illicit substances should be at least one year. A patient's stability (i.e., the presence of stable housing, relationships and finances) should be an important consideration in the decision to undertake voluntary withdrawal. Generally, patients who have been in MMT for two or more years will have better outcomes when tapered off methadone than those who start the tapering process before two years of treatment.

The patient should have a major role in deciding the rate of the taper in voluntary withdrawal.

Patients frequently request more rapid tapering than their physician may recommend, and it is important that physicians explain the dangers (primarily relapse risk) of rapid tapering. Involuntary withdrawal is sometimes necessary for violent or criminal behaviour, which results in safety risks or ineffectiveness of methadone treatment.

8.1.1 Standards for Voluntary Withdrawal

1. The MMT physician should warn the patient about the loss of opioid tolerance and the risk of toxicity if they relapse to opioid misuse.

8.1.2 Guidelines for Voluntary Withdrawal

1. The MMT physician should determine if the patient requesting taper is a good candidate for a successful methadone withdrawal, and discuss the risks and benefits of withdrawal with them.
2. For voluntary tapers, the MMT physician should taper patients slowly. The rate of the taper should be patient-driven, even if the patient desires a more rapid taper. The MMT physician should recommend a dose reduction schedule of 10% or less of the daily dose every 1 to 4 weeks (preferably every 2 weeks or more).
3. For voluntary tapers at lower dose (i.e., less than 50 mg), a slower dose change is recommended.
4. The taper should be slowed, stopped, or reversed at patient request (i.e., the patient experiences dysphoria, cravings, or withdrawal symptoms, or relapses to opioids or other drugs).

5. The MMT physician should offer to titrate the methadone dose back up if the patient requests it during voluntary withdrawal.
6. The MMT physician should see the patient regularly during the taper to assess the patient's mood and withdrawal symptoms, and to provide supportive counseling.
7. The MMT physician should offer to follow the patient for at least a few months after completion of the taper and offer to restart methadone if requested.

8.1.3 Standards for Involuntary Withdrawal

1. Once involuntary tapering has begun, the ingestion of all methadone doses must be witnessed.
2. The MMT physician should warn the patient about the loss of opioid tolerance and the risk of toxicity if they relapse to opioid misuse.

8.1.4 Guidelines for Involuntary Withdrawal

1. The MMT physician may transfer or involuntarily withdraw a patient from MMT if:
   a. The patient has been threatening or disruptive
   b. The patient is consistently non-adherent with safety related parts of the treatment agreement
   c. There is evidence that the patient's overall risk on MMT is equal to or higher relative to their risk if they were not on MMT
2. Immediate discontinuation of methadone without taper is possible in cases of extreme violence (e.g., threatening with a weapon, etc.).
3. The MMT physician should explain the reasons for involuntary withdrawal and offer to assist the patient to find another MMT physician if appropriate.
4. The MMT physician should decrease the methadone dose and assist the patient in seeking alternate care (e.g., an abstinence-based program) if a transfer is not feasible.
5. For an involuntary taper, the MMT physician should decrease the methadone dose at a rate of five to 10 mg every three to seven days until a dose of 50 mg is achieved. Below 50 mg, the rate of decrease should be no more than 5 mg every 3 to 7 days.
6. The MMT physician may use pharmacotherapy in the final 1 to 2 weeks of the decrease to relieve withdrawal symptoms.
7. The MMT physician should encourage the patient to engage with another health care professional or addiction treatment program for counseling and support.
8. The MMT physician should advise the patient's pharmacist and other health care providers regarding the involuntary withdrawal.

8.2 Voluntary Withdrawal

Patient-centered tapering has reasonably good success rates when undertaken in the context of medical and social stability as outlined below. It is not uncommon for patients to request withdrawal before they are clinically and socially stable. It is important to explore a patient's motivation in requesting withdrawal before it is medically indicated because often other reasons can influence the request (e.g., financial instability, family pressures, apprehension about a pending incarceration, etc.). A pre-tapering questionnaire has been found to be a useful tool in determining readiness for methadone tapering (See Appendix Q: Sample Tapering Readiness Questionnaire). In one study, 46% of subjects remained abstinent after an average of 2.4 years post-MMT (Cushman, 1978). More recent experience suggests a success rate that varies widely. In one review of patients who entered voluntary detoxification programs, the abstinence rate was between 22% and 48% (Kornor, 2005). Success rates are higher for patients who have been on MMT for 2 years or more (Cushman, 1981; Hubbard, Craddock, Anderson, 2003; Stimmel et al, 1978).

Factors leading to success in voluntary tapering are:

1. Long-standing abstinence from drugs of abuse.
2. No current mental illness
3. A supportive social network including the development of supportive relationships of non-users
4. Stable housing, finances and relationships
5. Resolution of legal issues and no connection to drug culture
6. Development of non-chemical coping skills
7. Optimized physical health

The rate of the taper should be negotiated with the patient and should be patient-driven. Voluntary withdrawal should be stopped* or *reversed at the patient's request for any reason.

Typical reasons will include withdrawal symptoms, social destabilization or relapse of substance use. In general, slow tapers are more successful than rapid tapers (Senay et al, 1977). The daily dose should generally be decreased by no more than 5-10 mg every 1 to 4 weeks (preferable every 2 or more weeks), and decreased no more than 10% of previous dose, particularly with daily doses below 50 mg. Tapering doses below 50 mg must proceed more slowly and carefully. In this case, gradual decreases of one to two mg every one to four weeks are generally used. The optimal rate at which tapering can be accomplished is highly variable between patients.

Tapering will likely trigger withdrawal symptoms as the lower dose range is reached, therefore overall stability, support and counseling are very important at this stage.

Patients should not be penalized for unsuccessful weaning from MMT.

8.3 Involuntary Withdrawal

8.3.1 Indications for Involuntary Withdrawal

The decision to withdraw a patient involuntarily from MMT should be documented in detail. The decision to initiate involuntary withdrawal should be based on reliable information with due consideration of the source.

Possible indications for involuntary withdrawal include:

- Threats to staff members or others
- Disruptive behaviour at the MMT physician's office or clinic or site where the methadone is being prescribed that has not been modified after being addressed
- Violent behaviour towards a staff member or others
- Non-compliance with patient treatment agreement and program expectations that results in a significant safety risk
- Repeated attempts at diversion of methadone
- High-risk for methadone overdose and attempts to reduce risk have failed. For example, the patient continues to use high doses of benzodiazepines or alcohol, has shown signs of sedation or has required medical treatment for an overdose, and refuses appropriate interventions (e.g., inpatient or outpatient benzodiazepine tapering)
- Ineffectiveness of methadone treatment, where there is no improvement in inappropriate use of opioids

- for example there has been no reduction in the use of intravenous opioids, and where it is evident that there has been no harm reduction. It is generally accepted that in order for physicians to justify the prescription of any medication, there must be a discernible and quantifiable benefit to the patient. For this reason, best practice requires prescribing physicians to identify and document objective benefits for each patient being prescribed methadone through the program.

Patients who are involuntarily withdrawn can be considered for readmission to MMT at a future date. Each MMT clinic or practice should have a policy outlining the requirements for readmission* to *MMT.

8.3.2 Process for Involuntarily Withdrawing a Patient

Recommendations to end the doctor-patient relationship effectively where MMT is being provided are as follows:

1. If possible, arrange a transfer to another MMT physician.
2. Communicate your decision clearly to the patient. This should include the details of a tapering schedule and/or end date of their methadone prescription.
3. Involuntary tapering may begin while the patient is searching for another physician.

Once an appointment for transfer is confirmed, involuntary tapering should be stopped at the current dose until the patient enters the new methadone program.

4. Once involuntary tapering has begun, all methadone doses must be daily witnessed ingestion. The MMT physician should decrease the methadone dose at a rate of 5-10 mg every 3 to 7 days until a dose of 50 mg is achieved. Below 50 mg, the rate of decrease should be no more than 5 mg every 3 to 7 days.
5. Provide the patient with reasonable help to find another MMT physician. Provide the CPSNL Methadone Program phone number for assistance in finding MMT physicians in the patient's community that are accepting new patients.
6. Have the patient sign acknowledgement that he/she is aware of the MMT termination or send the patient a registered letter, confirming termination with a return receipt requested and keep a copy in the medical record.
7. In extreme circumstances related to the safety of the staff or physician or others, a patient may be discharged without tapering.
8. When accepting a patient in transfer that has been involuntarily discharged, the new methadone 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 MMT physician's treatment concerns.

For more information on ending MMT physician-patient relationship, see the CPSNL Guideline: Ending the Doctor-Patient Relationship. Physicians may also contact the Canadian Medical Protective Association for advice in these circumstances.

CPSNL Guidelines :
http://www.cpsnl.ca/default.asp?com=Policies&m=340&y=&id=17

MMT patients who feel that they have been wrongfully dismissed can contact CPSNL with their concerns. If there are indications that a formal complaint is required, the matter can be referred to the investigations department of the College. The potential for dispute will be reduced if the MMT rules are made clear at the commencement of treatment.

9. Counseling and Case Management

Methadone programs should be more than a simple dispensing of methadone prescriptions.

9.1 Overview

Methadone programs should be more than a simple dispensing of methadone prescriptions. Most methadone patients struggle with a number of challenges, such as poverty, inadequate housing, lack of education, exposure to violence, poor nutrition, serious physical or mental health problems, interpersonal conflicts with self, family and friends, inability to secure and maintain employment, and involvement with the criminal justice system. These problems do not disappear just because the patient receives a daily dose of methadone. Methadone programs should be more than a simple dispensing of methadone prescriptions: they should incorporate a comprehensive biopsychosocial and, where appropriate to the patient, spiritual approach to help patients cope with their problems. When counseling is integrated into methadone maintenance programs, there are significant reductions in drug use. It is important for methadone prescribers not to adopt the perception that counseling is a task to be taken on exclusively by other staff or caregivers. All MMT physicians share in this significant responsibility as part of their overall mission to facilitate treatment and, ultimately, recovery.

9.1.1 Standards

1. The MMT physician shall provide counseling to willing patients or refer them to counseling services in the community while on MMT.
2. The MMT physician shall regularly document how the patient is doing in terms of their overall functioning.

9.1.2 Guidelines

None for this section.

9.2 Treatment Team

Collaborative practice in MMT is considered best practice. Ideally, the MMT patient should have access to a team that includes physicians, nurses, addiction services, pharmacists, and other care providers or counselors as needed. Although not all settings and communities are this ideal, the MMT treatment team (at minimum physician and pharmacist) can strive to achieve the best possible outcomes through a collaborative, inter-professional approach.

9.3 The Methadone Prescriber's Role

To assist the patient in meeting treatment goals, methadone prescribers must establish trusting, therapeutic relationships with their patients. Physicians need to create non-judgmental, collaborative environments in which patients feel safe to discuss their concerns. If positive relationships do not develop, the methadone maintenance program may have minimal benefit. 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. The patient, not the physician, should choose these treatment goals. 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, 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 prescribers should work with patients to develop treatment plans to meet these goals. This progress should be monitored and documented. Depending on each patient's circumstances, physicians should ideally work in collaboration with Addiction Services counselors, or may refer patients to independent counseling agencies or self-help groups such as Alcoholics Anonymous (AA) or Narcotics Anonymous (NA).

Many other specialized resources may be available to aid methadone patients. Physicians are expected to familiarize themselves and work in collaboration with community resources, such as addictions services, with the full spectrum of services available to their patient population through their local health authorities. They are also encouraged to refer their MMT patients to appropriate community treatment programs, support groups, and counselors. Whatever resources are chosen, physicians should be aware of the issues each patient is attempting to address and what progress has been made. This information should be incorporated into the patient's treatment plan.

The most important element of treatment is ensuring that the patient is engaged in the treatment, rather than the particular therapeutic model employed or the details of the treatment.

9.4 Case Management

Case management is defined as "a process that includes the designation of a primary worker whose responsibilities include the ongoing assessment of the patient and his/her problems, ongoing adjustment of the treatment plan, linking to and coordination of required services, monitoring and support, developing and implementing the discharge plan, and advocating for the patient" (Tschakodsky 2009) The concept of case management is an integral role of every family physician.

Where MMT is delivered within a program, under a collaborative team approach, the case manager may be a designated team member, rather than the MMT physician. Given that the context of care in which MMT is carried out in Newfoundland and Labrador, case management will vary from the independent family physician within a community practice to a physician within a defined MMT program working in a collaborative team, the concept of case management will be approached differently. In cases where the case management requirements are more than can be met by a family physician as the MMT prescriber in an office setting, the patient should be referred to addiction services who should provide support to MMT prescribers practicing within the region.

Case management should be offered regardless of where the individual is in the system (Ontario Addiction Services Advisory Council 2000).

The role of a case manager or a family physician includes the following activities:

1. Coordinating access to treatment
2. Providing information
3. Helping patients gain access to additional health and social services
4. Advocating for the patient

9.5 Therapeutic Factors

Methadone alone may lead to recovery, but to be optimally effective, MMT should be an integrated treatment approach that includes counseling and other supports that address the determinants of health.

9.5.1 Therapeutic Relationship

Research shows that a positive therapeutic relationship between a MMT physician and a patient has a helpful impact. Therapeutic approaches are most successful when there is a strong therapeutic alliance (Gossop et al. 2006; Martin et al. 2000; Senay et al. 1977). This involves the MMT physician creating a non-judgmental, collaborative environment whereby patients feel safe to discuss their feelings and concerns. Particularly where there are complex psychosocial problems, the MMT physician will need to draw on the support of formal and informal referral and realize the limits of what they can provide. If a MMT physician is not able or prepared to provide counseling, it is essential to connect the patient with services in the community.

Non-judgmental trusting collaborative physician-patient relationships are essential for positive results.

9.5.2 Extra Therapeutic Factors

Social determinants of health (extra-therapeutic factors), such as housing, income and social support networks, can greatly affect a person's mental health (Senay et al. 1977). Providing counseling and case management to MMT patients can be complex, as patients may need help making changes in how they use substances, they may have financial, housing, legal, and health problems, and many have histories of trauma, mental health problems or relationship difficulties. Instability or difficulty in one or more of the following areas may indicate a need for more intensive counseling and help. These services are available from addiction services personnel employed at various locations throughout the province. MMT physicians should consider a referral to Addiction Services.

Medical and wellness issues may include:

1. Identification and treatment of concurrent mental illness
2. Chronic physical health problems (Hepatitis C virus [HCV], human immunodeficiency virus [HIV], birth control)
3. Pregnancy
4. Issues of abuse – physical, sexual, emotional – and trauma
5. Parenting and family counseling
6. Changing drug and alcohol use
7. Lifestyle changes such as smoking, nutrition, exercise, leisure time

Life skills and practical help may include:

1. Securing basic necessities, such as housing, food, clothing
2. Legal assistance
3. Life skills
4. Coping with stress

5. Social isolation
6. Chaotic lifestyle (frequently missed appointments or doses)
7. Stopping drug use and preventing relapse

Practical support may include:

1. Support and someone to talk to
2. General counseling
3. Help with referrals to community resources
4. Filling out forms and applications, providing letters

9.5.3 Concepts of Recovery

Recovery refers to the ways in which people with mental health and/or addiction problems experience their lives through focusing on positive, including health, hope, choices, equity, respect, supports and optimizing their quality of life. More specifically, recovery is about empowerment (having control over one's life), self-determination and personal responsibility, having one's expertise valued, reaching one's potential, engaging in meaningful activities, such as education and work, being included in community life, and having a voice in one's treatment plans.

Excerpted from *Overview of Health Promotion*, accessed on CAMH Knowledge Exchange portal December 2010.

> **Overview of Health Promotion**
> http://knowledgex.camh.net/amhspecialists/promotion/Pages/default.aspx

Not all opioid-dependent patients will do well on methadone. Like any other medical treatment, there are risks and benefits associated MMT.

Methadone prescribers must clearly document the benefits derived from MMT in each patient's chart, and also develop and record a treatment plan that outlines how further benefits are to be achieved. Documenting the benefits of MMT goes beyond the basic requirements of a medical record as outlined in the CPSNL By-Law No. 6: Medical Records.

> **Download** CPSNL By-Law No. 6: Medical Records
> (http://www.cpsnl.ca/default.asp?com=Bylaws&m=292&y=&id=9)

In addition to recording the dose of methadone provided at each visit, some reference to parameters of benefit and current treatment plans should be recorded.

9.5.4 Benefits of Methadone Maintenance Treatment

Methadone prescribers may find this list useful for assessing their patients' progress and for formulating and monitoring treatment plans:

- Reduced or discontinued use of intravenous opioids
- Reduced or discontinued use of other mood-altering drugs
- Improved mental and physical health
- Improved engagement with primary care

- Reduced incidence of concomitant infections such as endocarditis, osteomyelitis, and cellulitis, with consequent reduced need for hospitalization
- Reduced emergency room visits for drug-related complications
- Improved nutrition and weight gain
- Improved HCV and HIV status
- Improved pregnancy outcomes
- Improved mental health status
- Improved rating on the DSM-IV-TR Global Assessment of Functioning (GAF) Scale
- Reduced involvement with the criminal justice system
- Improved living situation (End-stage opioid dependence often results in homelessness or unsafe living conditions. Methadone maintenance patients should be encouraged to seek drug-free accommodation, as this is essential for successful recovery. The definition of an improved living situation might include an environment with sober friends, safe long-term, drug-free housing or housing which supports recovery, as well as other forms of supportive housing)
- Improved social and personal relationships
- Improved vocational and employment opportunities (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)

Remember to revise and update your patients' treatment plans as program goals and benefits change.

9.5.5 Counseling Techniques and Skills

There is evidence of the impact of counseling. Recent studies recommend that MMT physicians be willing and able to provide counseling to their MMT patients (Drucker et al. 2007). In a recent survey of MMT patients in Ontario (Senay et al. 1977), 27% indicated they received counseling from MMT physicians (either alone or in addition to other support), 18% received counseling from a nurse and 12% received counseling from a psychiatrist (either alone or in addition to services from another agency).

Counseling happens across the continuum of care, from screening and assessment through treatment and relapse prevention. Most change happens in early treatment. Types of counseling that have proven effectiveness in addictions work include Motivational Interviewing (MI) and Cognitive Behaviour Therapy (CBT).

MI is a counseling style that recognizes and resolves patient ambivalence to prepare patients to change addictive behaviours. MI elicits change statements and goals from the patient, rather than the counselor. It has been shown to be particularly helpful in working with people who use substances (Burke et al. 2002). This method focuses on patient's experiences, draws on their concerns, perspectives and values, and encourages patients to evaluate their own life choices and explore the consequences of their choices in a non-judgmental way.

CBT is a talk therapy that leads to understanding the relationship between thoughts, behaviours and feelings. It is increasingly identified as the "gold standard" for psychotherapy in the field of

addictions. CBT has been shown to be effective for people of all ages, and for people of different levels of education, income and various cultural backgrounds. It has also been shown to be effective in either individual or group formats.

If appropriately educated and supported (and with the patient's consent), the patient's family can be a valuable resource for the patient and the MMT physician. The MMT physician can also play a valuable role in encouraging and facilitating access to supports and services, such as relapse prevention programs in the community.

Substance-dependent patients are often described as lacking motivation to change or having fear of change, especially if that change requires some self-organization. Methadone prescribers can effectively use frequent, brief interventions to instill motivation in patients who lack self-motivation.

The following are examples of positive brief interventions that address different barriers to change in patients' lives:

Building a therapeutic relationship:

- Demonstrate sustained interest and concern for patients' progress
- Schedule regular visits and ensure that two-way communication exists

Education:

- Provide factual drug information
- Educate patients regarding the symptoms of impending relapse, such as exhaustion, complacency, impatience, dishonesty, self-pity, frustration, depression and argumentativeness
- Discuss behaviours such as denying, minimizing, rationalizing, intellectualizing and compartmentalizing

Goal planning:

- Consider all areas of patients' lives, not just issues around drug use
- Prepare and document avoidance and "escape plans" to deal with risky situations that could potentially lead to relapse of drug use
- Identify and help remove barriers to change (such as the need for childcare or transportation)
- Remind patients that it is better to reach a modest goal than to fail to reach a more ambitious target and coach patients to take achievable steps on the road to recovery

Promoting self-awareness and positive behaviours:

- Identify internal and external triggers for relapse
- Avoid dwelling on failures, rather help patients take pride in and build on their successes
- Encourage harm-reduction behaviour
- Encourage the development of self-esteem, which is the primary ingredient necessary for any successful therapy

9.6 Community Resources

See Appendix N: Resources

10. MMT with Concurrent Mental and Physical Disorders

MMT Physicians must be skilled in the identification of management of conditions that are common in opioid dependent patients, such as physical and mental health disorders

10.1 Overview

MMT physicians need to be skilled in the identification and management of conditions that are common in opioid-dependent patients, such as medical and mental health disorders. All patients should have an identified primary care physician. The MMT physician should encourage the patient to see their primary care physician regularly for ongoing preventive care, screening and chronic disease management.

10.1.1 Standards

1. The MMT physician shall not prescribe methadone for pain without a Health Canada exemption unless the primary focus of the patient's care is treatment of opioid dependence rather than pain management. In this circumstance, CPSNL MMT Standards and Guidelines should be followed with appropriate modification for split dosing.

10.1.2 Guidelines

1. The MMT physician should encourage patients to attend a primary care physician or team for ongoing age-appropriate screening and chronic disease management.
2. The MMT physician should have open and regular communication with the patient's primary-care physician.
3. MMT physicians should screen patients for hepatitis C and HIV, and offer referral and treatment when clinically indicated.
4. The MMT physician should assess patients periodically for alcohol use through an alcohol consumption history. Screening questionnaires and laboratory measures might also be considered.
5. For patients with acute pain that warrants short-term opioid therapy, MMT physicians may temporarily split the methadone dose with an additional 10-15 mg evening dose, or prescribe opioids in addition to methadone.
6. If opioids are prescribed for acute pain, the MMT physician should choose an opioid that the patient has not misused in the past, and dispense the opioid in small amounts (controlled dispensing). The MMT physician should limit the prescription to the number of days that opioids are typically needed for that particular acute pain condition.
7. MMT physicians should become familiar with the *Canadian Guideline for Safe and Effective Opioid Use in Chronic Non-Cancer Pain*.

   http://nationalpaincentre.mcmaster.ca/opioid/index.html

8. The MMT physician may prescribe methadone in split doses for patients with severe chronic pain who require opioids. Usually this should only be done after the patient is on a stable once-daily dose and is receiving five or six take-home doses per week.
9. The MMT physician should only attempt long-term opioid therapy for methadone patients with chronic non-cancer pain if:
    a. The patient has severe pain from a well-documented diagnosis of a serious nocioceptive or neuropathic condition that would usually require opioid analgesics.

       Note: Common conditions such as fibromyalgia or low back pain do not warrant combination methadone and opioid therapy.

    b. The patient has had insufficient analgesic benefit from an adequate trial of non-opioid treatments and from a trial of split methadone dosing.
10. If opioids are prescribed in addition to methadone, the recommended opioids for most patients are codeine and tramadol, followed by morphine. The MMT physician should use strategies to minimize diversion and misuse. The MMT physician should periodically attempt a trial of opioid tapering, particularly in patients on higher opioid doses who continue to report severe pain.
11. The MMT physician should periodically screen and assess MMT patients for anxiety and mood disorders and refer to a mental healthcare professional if they have failed to respond to primary-care treatments.
12. The MMT physician should attempt to decrease long-term benzodiazepine treatment to a lower dose for MMT patients, particularly if they:
    a. are on multiple daily doses
    b. show signs of misuse
    c. are elderly
    d. are on a high methadone dose
    e. are on other sedating drugs

10.2 Physical Disorders

10.2.1 Infectious Disease

10.2.1.1 Hepatitis C and HIV

Hepatitis C treatment with interferon and ribavirin can be successfully integrated into MMT. Adherence to anti-retroviral treatment for HIV is higher in patients on MMT than those not receiving MMT (Harris et al. 2010, Uhlmann et al. 2010).

10.2.2 At-Risk Drinking

At-risk drinking and alcohol dependence are common among MMT patients (Backmund et al., 2003, Hillebrand et al. 2001). Excessive alcohol use accelerates liver damage in patients with Hepatitis C (Szabo et al., 2010), although the impact of moderate alcohol consumption is not

well understood (Cheung et al., 2010). Alcohol also contributes to substance-induced mood, anxiety and sleep disorders. Alcohol interacts with methadone causing sedation, risk of overdose, aspiration, accidents, violence, and other adverse events.

Methadone treatment does not appear to significantly reduce alcohol consumption in the long-term (Anchersen et al. 2009; Caputo et al. 2002; Srivastava et al. 2008), which suggests that methadone programs do not pay enough attention to the issue. Evidence suggests that counseling about alcohol use is effective in methadone patients (McCusker 2001).

MMT physicians should be aware of special considerations involved in managing alcohol problems, such as:

Low-risk drinking guidelines

The current guidelines recommend no more than 14 standard drinks per week for men and nine per week for women. Lower limits are recommended for patients with Hepatitis C.

Pharmacotherapy

The first-line medication used to treat alcohol dependence, naltrexone (ReVia ®) is contraindicated in patients on methadone. Available alternatives include disulfiram and acamprosate.

Alcohol withdrawal

To avoid benzodiazepine toxicity, methadone patients in alcohol withdrawal should be given smaller doses of lorazepam (e.g., 1-2 mg) rather than diazepam.

10.2.3 Hepatic, Renal, and Respiratory Disease

Hepatic Disease

- While stable liver dysfunction does not appear to affect methadone levels (Beauverie et al., 2001; Novick et al. 1985), MMT physicians have seen methadone patients who have become very sedated when admitted for acute decompensated cirrhosis. The MMT physician should consider decreasing the dose in this circumstance, and benzodiazepines should be avoided. The half-life of benzodiazepines can be prolonged in hepatic dysfunction, and benzodiazepines can trigger encephalopathy. The QT interval should be monitored as liver dysfunction is a risk factor for Torsades de Pointes arrhythmias. (Ehret et al. 2006).

Renal Disease

- Evidence suggests that the metabolism of methadone is not affected by renal insufficiency (Kreek et al., 1980, Murtagh et al, 2007). Nonetheless, patients in acute renal failure should be monitored closely for signs of methadone toxicity.

Respiratory Disease

- Tolerance to the respiratory depressant effects of methadone develops very slowly and incompletely. Methadone patients who develop an acute, serious respiratory illness (e.g., pneumonia, COPD exacerbation) should be closely monitored for both worsening respiratory function and methadone toxicity. Abrupt cessation of methadone should be avoided, as withdrawal may cause cardiorespiratory complications due to anxiety and agitation (Friedman et al. 2003; Kienbaum et al. 1998).

Cardiac Disease

- Patients who have cardiomyopathy due to ischemia or other causes are often at higher risk for arrhythmias, therefore their QT interval should be closely monitored and their dose adjusted if necessary. Rapid methadone tapering should be avoided in patients with coronary artery disease as it can trigger cardiorespiratory instability.

10.2.4 Acute Pain

MMT patients are tolerant to the analgesic effects of opioids (Doverty et al., 2001), so if they experience severe acute pain they may require opioids in higher or more frequent doses than non-tolerant patients.

In MMT patients who are eligible for take-home doses and have severe pain unresponsive to non-opioid treatments, temporarily adding an afternoon or evening methadone daily dose (e.g., 10-15 mg) may be helpful. If this is ineffective or not advisable, then the physician might consider a short-term opioid prescription. MMT patients' views on opioid use should be discussed before prescribing; some MMT patients are concerned that opioids will trigger a relapse and would prefer non-opioid analgesics. If possible, the MMT physician should avoid the MMT patient's previous opioid of abuse or an opioid commonly abused in the community. For most MMT patients, morphine is preferred over oxycodone or hydromorphone.

10.2.5 Chronic Non-Cancer Pain

Chronic non-cancer pain is common in MMT patients (Rosenblum et al., 2003). MMT physicians who prescribe methadone are encouraged to become familiar with the *Canadian Guideline for Safe and Effective Opioid Use in Chronic Non-Cancer Pain.* However, MMT patients with CNCP present clinical challenges that require special consideration when prescribing opioids.

Table 12: Overview of Pain Management

Pain Condition	Management
Mild to moderate Common conditions such as fibromyalgia, low back pain.	Non-opioid treatments
Severe nocioceptive or neuropathic pain condition that usually requires opioid therapy.	First-line: Non-opioid treatments Second-line: Split methadone dose Third-line: Codeine or tramadol Fourth-line: Potent opioids e.g., morphine.

10.2.5.1 Methadone for Analgesia

MMT physicians cannot prescribe methadone as an analgesic for non-addicted patients with chronic pain, unless they have a special exemption from Health Canada. This exemption is independent of the exemption for methadone as a treatment of addiction.

Controlled trials have found that methadone is of comparable effectiveness to morphine as an analgesic (Bruera et al. 2004; Mercadante et al. 2008). While the duration of analgesic action of methadone is no more than eight hours (Grochow et al., 1989), an initial trial of once daily dosing is suggested. Patients with concurrent pain and opioid addiction often experience substantial pain relief once methadone treatment is initiated. When an optimal dose is reached, the dose may be split if the patient continues to experience severe pain unrelated to withdrawal several hours after the morning dose. Patients should be eligible for 5-6 take-home doses before receiving a split dose. Consultation with a physician experienced in methadone and pain should be considered.

10.2.5.2 Opioids in Combination with Methadone

Research to date has not examined the safety or effectiveness of methadone in combination with other opioids for opioid-dependent patients with chronic non-cancer pain. Furthermore, long-term opioid prescribing in MMT patients makes it difficult to prevent and detect opioid misuse and diversion. Therefore, opioids should only be used if there is strong likelihood of benefit, (i.e. patients with serious, well-defined nociceptive or neuropathic conditions who have not responded to first-line non-opioid treatments or to split methadone dosing). Use of opioids is not justified in MMT patients with common pain conditions such as fibromyalgia or low back pain.

If split methadone doses are ineffective, then codeine or tramadol can be tried. If more potent opioids are required, in many cases the MMT physician should consider using morphine rather than oxycodone or hydromorphone (Rauck et al. 2007). Evidence suggests that oxycodone and hydromorphone have a higher risk of addiction

and overdose than morphine, and therefore the latter is preferred in high-risk patients. Oxycodone is a common drug of abuse in Ontario, and it is the most common opioid involved in fatal opioid overdoses (Dhalla et al, 2009). See *Canadian Guideline for the Safe and Effective Opioid Use in Chronic Non-Cancer Pain.*

http://nationalpaincentre.mcmaster.ca/opioid/index.html

10.2.5.3 Preventing Misuse and Diversion in Patients on both Methadone and Opioids

MMT patients do not always inform their MMT physician if they are receiving opioids from another physician. Collaboration and communication between the MMT physician and pharmacist can enhance knowledge of other medications the MMT patient may be taking. For some MMT patients, ongoing UDS provides appropriate structure while on regularly prescribed opioids. Until a prescription opioid monitoring system is in place, MMT physicians have few options other than to:

- communicate with the patient's non-MMT physicians
- obtain records from emergency department visits and hospitalization
- advise non-MMT physicians to order UDS for methadone when prescribing opioids, particularly if they do not know the patient well or if the patient is at high risk for opioid misuse.

If the MMT physician knows that another physician is prescribing opioids for the patient, several strategies can be implemented to minimize opioid diversion and misuse. The opioid can be dispensed along with the methadone take-home doses. Pill counts and regular urine drug screening can also be helpful. Close communication with the patient's opioid prescriber is advised to prevent dangerous drug combinations.

10.2.5.4 Opioid Tapering

Tapering is indicated for patients who report severe pain and pain-related disability despite reasonable opioid doses. Research has demonstrated that these patients experience reduced pain and improved mood and functioning with opioid tapering (Baron et al. 2006, Crisostomo et al. 2008, Hooten et al. 2007)**.**

10.3 Mental Illness

10.3.1 Anxiety and Mood Disorders

The prevalence of anxiety and mood disorders is several times higher in MMT patients than in the general population (Callaly et al. 2001; Mason et al. 1998). Co-occurrence of substance abuse and psychiatric problems is frequently diagnosed in patients in MMT, particularly Axis I and Axis II disorders and depressed MMT patients can be more sensitive to opioid withdrawal (Astals et al. 2008; Cacciola et al. 2001; Callaly et al. 2001; Elkader et al. 2009). To date there is little evidence to support the use of antidepressants in treating mood disorders in MMT patients (Carpenter et al. 2004; Dean et al. 2002). Therefore, MMT physicians might consider

referring MMT patients for more intensive assessment and treatment if they have persistent depression and anxiety despite an initial trial of pharmacotherapy.

10.4 Benzodiazepines

Benzodiazepine use in MMT patients is associated with increased psychological distress, risk for overdose, higher risk of suicidal behaviour, violence, impaired attention and memory, impaired driving and risk for continuing poly-drug use (Bleich et al. 2002; Brands et al. 2008; Caplehorn & Drummer, 2002; Darke et al. 2010; Darke et al. 2009; DeMaria et al. 2000; Man Lan-Ho et al. 2004) Furthermore inconsistent results regarding the impact of benzodiazepine use on treatment retention have been reported; negative impact (Peles et al. 2010) or no impact on treatment retention (Kellogg et al. 2006). As well, an observational study documented reduced symptoms of depression in MMT patients who were tapered off benzodiazepines and started on antidepressant therapy (Schreiber et al. 2008).

WHO Guidelines (2009) suggest that gradual withdrawal from benzodiazepines may be necessary for benzodiazepine users in MMT programs.

11. Methadone Toxicity

The most likely time for a patient to experience toxicity is during the early stabilization phase. Due to its long half-life, the effect of methadone is cumulative and toxicity may develop several days after a dose change. Cross-tolerance between methadone and other opioids is unpredictable, so a patient who is tolerant of another opioid is still at risk for methadone toxicity.

11.1 Overview

Methadone toxicity presents a serious challenge to MMT physicians.

Opioid toxicity leading to overdose is characterized by a decreased level of consciousness, respiratory depression and pinpoint pupils. Two features of methadone toxicity make interpretation of these signs difficult:

- Definite signs of methadone toxicity may not become apparent for 5-9 hours after the overdose (Caplehorn and Drummer 2002; Lovecchio et al. 2007).
- MMT patients who have had an overdose may appear relatively alert during conversation, succumbing to respiratory depression during sleep (Caplehorn 1999).

11.1.1 Standards

None for this section

11.1.2 Guidelines

1. The MMT physician should assess patients in person or refer them to the emergency department (See Appendix R: Emergency Department Management of Methadone Overdose) if they might have taken a dose above and beyond what would be considered a safe dose, given their underlying tolerance, concurrent medication use, and health status.
2. If, after assessment (see Section 11.2.2), the MMT physician is concerned that the patient is at imminent risk for methadone toxicity, the MMT physician should take the following steps:
    a. Explain the risks of methadone overdose, including respiratory depression and death, and advise the patient (or if the patient lacks capacity, advise the patient's substitute decision maker, if available) that an ambulance is being called.
    b. Ensure a staff member keeps the patient awake until the ambulance arrives.
    c. Consider seeking an order of the court for an involuntary mental health assessment, under the *Mental Health Care and Treatment Act,* if the patient refuses to attend the emergency department.

11.2 Dosing and Assessment for Possible Methadone Toxicity

11.2.1 Definition of a toxic dose

Reasonable dose increases usually range between 10-15 mg every 3-5 days. For example, if a patient has consistently been on 50 mg/day for several weeks and then receives 65 mg by mistake, this would be considered within the range of a “reasonable” dose increase for that patient. However, if the patient was just initiated on 30 mg the day before and then receives 45 mg on the second day, they could be at risk of methadone toxicity.

If the exact amount ingested is not known with certainty, it is safest to manage the patient as if they took an overdose, even if the patient reports that he/she is alert and only took a "small amount".

The risk of toxicity is determined not just by the amount of the extra dose but by the patient’s underlying tolerance and underlying health status. Even ‘small’ extra doses of 15-20 mg can cause toxicity during the first two weeks of methadone titration, or if the patient is elderly or has a respiratory illness.

11.2.2 Assessment of the MMT patient who may have taken a toxic dose

If the patient is currently at the MMT physician’s office or clinic, the MMT physician should engage the patient in conversation for at least five minutes, as an overdosed patient would have trouble maintaining alertness for more than a few minutes. During the conversation, observe for sweating, emotional lability, slurred or drawling speech, and “nodding off”. If possible, the patient should also be observed when not engaged in conversation. Falling asleep, ‘dozing’ or ‘napping’ could indicate toxicity even if the patient is easily rousable. If possible, physiological measures such as decreased blood pressure, heart rate, and slow/irregular breathing should also be assessed. Remember that the peak effect of the methadone is apparent several hours after ingestion (Wolff 2002).

If the patient is at home, ask family members to describe the patient’s sleep. Loud snoring and apneic episodes during sleep could indicate a life-threatening overdose.

11.3 Patient Referral to the Emergency Department for Overdose

If possible, the MMT physician should speak directly with the attending emergency department physician or nurse, advising them that:

1. The patient should be observed for a minimum of 10 hours.

2. The patient should be discharged only if they have not displayed any signs of lethargy or sedation during that time.

If the MMT physician decides not to call the ambulance, a reliable adult should accompany the patient to the emergency department. The person must understand the life-threatening nature of the overdose and the dangers of refusing emergency department management.

11.4 Refusal to go to Emergency Department

The MMT physician should carefully document in the patient chart when a patient refuses to go the emergency department on his/her advice. Explain to the patient and their partner or family member if available that the patient is at risk of respiratory depression and death, especially if they fall asleep. Advise the patient not to use any other substances or medications. Advise the patient that a court order for an involuntary mental health assessment, under the *Mental Health Care and Treatment Act,* may be sought if the patient refuses to attend the emergency department.

12. MMT Considerations during Pregnancy

Pregnant opioid dependent women are at increased risk of obstetrical and medical complications due to repeated cycles of opioid intoxication and withdrawal

12.1 Overview

Pregnant opioid-dependent women are at increased risk of obstetrical and medical complications due to repeated cycles of opioid intoxication and withdrawal. Pregnant opioid-dependent women have higher rates of premature delivery and infants with low birth weight leading to higher rates of infant morbidity and mortality (Finnegan 1978; Hulse et al. 1997, 1998; Kandall et al. 1977; Little et al. 1990; Rementeria and Nunag 1973; Stern 1966; Stimmel et al. 1982; Vucinovic et al. 2008; Wilson et al. 1981). Morbidity and mortality have been attributed to the direct effect of the drug itself, but are also secondary to other associated lifestyle factors such as poor nutrition, inadequate prenatal care attendance and concomitant substance use such as alcohol and tobacco (Fricker and Segal 1978, Hulse et al. 1997, Vucinovic et al. 2008).

The benefits of MMT during pregnancy include improved prenatal care, nutritional status and social stability leading to increased likelihood of maternal custody, as well as, reduced incidence of pre-term delivery, low birth weight and infant mortality (Chang et al. 1992; Kaltenback and Finnegan 1992; Wilson et al. 1981).

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

12.1.1 Standard

1. The MMT physician shall offer, on an urgent basis, MMT to opioid-dependant pregnant patients.

12.1.2 Guidelines

1. MMT physicians should ensure pregnant opioid-dependent patients are counseled regarding the risks and benefits of MMT during pregnancy.
2. The MMT physician should consider inpatient initiation during pregnancy in order to monitor for withdrawal severity and fetal distress.
3. The MMT physician should aim for a maintenance dose of methadone that keeps the patient comfortable for 24 hours and helps maintain abstinence.
4. MMT physicians should consider split dosing during pregnancy as an alternative strategy to increasing the methadone dose in the third trimester.
5. The MMT physician should assess the MMT dose for adjustments, especially for dose increases during the third trimester of pregnancy to prevent maternal withdrawal symptoms.

6. The MMT physician should consider dose replacement after reported emesis in pregnant women.

7. The MMT physician should consider tapering and detoxification in selected patients based on clinical and social stability, previous good response to tapering, and no concurrent psychiatric disorders or addiction to other substances.

8. The MMT physician should assist the MMT patient in obtaining adequate prenatal care by referring for obstetrical care as soon as pregnancy is identified.

9. The MMT physician should ensure there is open communication between the methadone and obstetrical physician, or family doctor if a patient does not have an obstetrical physician, regarding the use of MMT during pregnancy and planning for labour and delivery.

10. The MMT physician should make arrangements to ensure the pregnant MMT patient receives her regular daily methadone dose during labour and delivery.

11. The MMT physician should monitor the MMT patient closely for symptoms of methadone intoxication and mood disorders during the postpartum period.

12. The MMT physician may need additional visits with the patient during the immediate postpartum period to provide support during this transition phase.

13. The MMT physician should encourage breastfeeding during MMT.

14. The MMT physician may have a duty to report to a child protection agency, depending on the mother's length of time in treatment, the stability of substance use, and social situation. See section 12.8 for further information. The MMT physician may also contact the Canadian Medical Protective Association for advice in these circumstances.

12.2 Effects of Methadone during Pregnancy

Methadone crosses the placenta, but has not been found to be teratogenic. There is weak evidence linking strabismus to opioid use during pregnancy, especially with methadone exposure in utero (Gill et al. 2003; Nelson et al. 1987)**.**

To date, no conclusive long-term study has been published about the long-term effects of neonatal exposure to methadone (Chasnoff et al. 1982; Hans 1989; Hunt et al. 2008; Kaltenbach and Finnegan 1987; Lifschitz et al. 1985). Environmental factors and caregivers can play a significant role in mediating these effects of methadone exposure on infants' growth and development.

The most significant risk of methadone exposure during pregnancy is neonatal withdrawal also known as neonatal abstinence syndrome (NAS) (Kaltenbach & Finnegan 1986)**.** Up to 85% of newborns exposed to methadone experience withdrawal symptoms and signs (Bell and Lau 1995; Finnegan et al. 1975) such as:

1) central nervous system (CNS) hyperirritability (high-pitched cry, increased muscle tone, sleep disturbances, tremors, seizures)
2) gastrointestinal dysfunction (poor feeding, regurgitation, vomiting, loose stools)

3) metabolic, vasomotor, and respiratory disturbances (sweating, recurrent sneezing, yawning, fever).

Withdrawal usually begins within 72 hours of birth, but late presentations (up to 2-4 weeks after birth) have been reported (Finnegan and Kaltenbach 1992) and symptoms may last for several weeks or months.

12.3 MMT during Pregnancy

12.3.1 Inpatient vs Outpatient

See Appendix M: Protocols for MMT and Pregnancy.

There are no studies to demonstrate the efficacy and safety of inpatient over outpatient stabilization. However, inpatient stays allow for investigations of maternal health and prenatal status and referral to others (e.g., social worker, obstetrical care provider).

Inpatient initiation is not always feasible due to personal factors (e.g., fear of medical personnel and hospitals, childcare issues and lack of support from family or partner) or systemic factors (e.g., unavailability of methadone in the hospital and limited staff experience). However, if a pregnant woman complains of uterine irritability (e.g., abdominal cramping and bleeding) during outpatient initiation, hospital admission is indicated.

12.3.2 Methadone Dosing During Pregnancy

12.3.2.1 Establishing a Maintenance Dose

An appropriate maintenance dose should be determined for each individual. A clear relationship between maternal methadone dose and the severity of Neonatal Abstinence Syndrome (NAS) has not been established (Berghella et al. 2003; Dashe et al. 2002; Doberczak et al. 1993; Kaltenbach and Comfort 1997) due to the potential effect of other factors such as concomitant drug use (e.g. cocaine, benzodiazepines) on neonatal withdrawal (Berghella et al. 2003; Mayes and Carroll 1996). The risks of illicit opioid use outweigh the potential risks of higher methadone doses.

12.3.2.2 Dose Splitting During Pregnancy

Twice-daily methadone dosing has been associated with sustained plasma methadone levels and fewer withdrawal symptoms resulting in improved treatment compliance and decreased use of other illicit substances (Swift et al. 1989, Wittmann and Segal 1991). Split doses have also been shown to cause less suppression of fetal behaviour than with single daily dosing which has demonstrated decreases in both fetal movements and fetal breathing after dosing (Jansson et al. 2009; Wittmann and Segal 1991). Therefore, when pregnant women continue to experience withdrawal symptoms with single daily dosing, split dosing (i.e., every 12 hours) can be considered. Women need to meet stability criteria for take-home doses or arrangements can be made with the pharmacy to provide an evening observed dose.

12.3.2.3 Dose Adjustments during Pregnancy

Women in MMT prior to conception can continue on their pre-pregnancy dose during the first and second trimesters (Finnegan 1991). Methadone clearance rates gradually increases from the first to the third trimester resulting in lower mean serum methadone levels as the pregnancy progresses (Drozdick et al. 2002; Jarvis et al. 1999; Wolff et al. 2005). This change in methadone clearance has been attributed to different factors such as increased methadone metabolism during pregnancy, increased maternal renal elimination, increased volume of distribution and tissue binding, and additional metabolism by placenta and fetus (Pond et al. 1985, Swift et al. 1989). Small increments in methadone dose later in pregnancy will be required.

12.3.2.4 Managing Vomited Doses

See Section 5.10 Vomited Doses.

12.4 MMT Tapering or Withdrawal during Pregnancy

Recent clinical experience with MMT detoxification (i.e., methadone-assisted withdrawal) has not demonstrated any increased incidence of obstetrical complications or adverse neonatal outcomes during the first, second or third trimesters (Blinick et al. 1969; Dashe et al. 1998; Jones et al. 2008; Luty et al. 2003; Maas et al. 1990). However, MMT detoxification has been associated with clinical instability and a high risk of relapse to substance use requiring resumption of MMT.

There is limited guidance in terms of the rate of methadone tapering or detoxification. Some studies have proposed reducing the dose by 1-2 mg/day as an inpatient or by 2-10 mg every 1-2 weeks as an outpatient (Archie 1998; Finnegan 1991; Jarvis and Schnoll 1994; Kandall et al. 1999). However, these numbers are not based on systematic studies. In pregnancy, the dose should be decreased slowly by 5-10% per week. This process should be stopped if the pregnant woman reports any adverse outcomes such as relapse to drug use, increased cravings, intolerable withdrawal symptoms or obstetrical complications.

Motivated women who have a short addiction history, are medically and socially stable with a good support network and have no concurrent psychiatric disorder may have better outcomes following detoxification.

12.5 Prenatal Care for MMT Pregnant Patients

The addition of on-site prenatal care has been shown to improve attendance and pregnancy outcomes (Chang et al. 1992). Binder and Vavrinkova showed that methadone substitution treatment provides pregnant women with greater social stabilization and prenatal care (Binder and Vavrinkova 2008). Therefore, comprehensive care that provides MMT and prenatal care is the most effective approach in increasing patient retention and reducing adverse neonatal outcomes (Ellwood et al. 1987).

12.6 Intrapartum Management for MMT Pregnant Patients

Methadone will not provide pain relief during labour and additional analgesia will be required.

12.7 Postpartum Management for MMT Patients

12.7.1 Dosing

A few days or weeks postpartum, the MMT patient may find her established dose of methadone is too high. If so, it should be decreased by 5-10 mg every week based on clinical symptoms until a new stable dose is reached. The MMT physician should consider the risk of relapse to illicit opioids prior to beginning the decrease.

12.7.2 Support

Mothers often feel extremely guilty if the infant exhibits symptoms of opioid withdrawal requiring treatment and an extended hospital stay. The services of public health nurses and attendance at drop-in centers and parenting classes should be encouraged.

12.7.3 Breastfeeding

Methadone enters the breast milk in very small amounts that are unlikely to be clinically significant (Glatstein et al. 2008; Jansson et al. 2004)**.** The mean daily amount of methadone ingested by infants ranges between 0.01 and 0.05 mg depending on the maternal methadone dose. This amount is not sufficient to prevent neonatal absence syndrome (NAS) and the infant still requires additional opioid treatment for NAS.

12.7.3.1 Breastfeeding and Hepatitis C

No studies have demonstrated transmission of HCV through breast milk alone to infants (Wong and Lee, 2006)**.** Breastfeeding by women who are infected with hepatitis C (HCV) is considered safe.

12.8 Reporting to Child Protection Agencies

Any health care professional who has reasonable grounds to suspect that a child is, or may be, in need of protection has a legal duty to report this suspicion. In Canada, the fetus is not legally recognized as a person and as such, the obligation to report only applies once the child is born. Prenatally, health care providers may contact child protection services after discussion and with consent from the pregnant woman. Patients should be encouraged to self-report during the prenatal period in order to increase self-efficacy, dignity and stability while promoting an open and informed decision-making by child protection authorities. However, immediate reporting if the pregnant woman has children in her care and there is a child protection concern in relation to those children. The MMT physician should consider contacting the Canadian Medical Protective Association for advice in these circumstances.

13. MMT in Federal/Provincial Correctional Facilities

Incarcerated individuals who are current MMT patients at the time of incarceration are continued on MMT for the duration of their stay.

13.1 Overview

Incarcerated individuals who are current MMT patients at the time of incarceration are continued on MMT for the duration of their stay.

The initiation of MMT in custody would require collaboration with a community MMT physician who would have to agree that the incarcerated individual is a suitable candidate for MMT and would be prepared to accept the individual in transfer to his/her MMT practice upon release.

13.1.1 Standards

1. The institutional MMT physician shall ensure the patient signs a Treatment Agreement.
2. The institutional MMT physician shall ensure the Treatment Agreement and medical history is kept as part of the medical file.
3. The institutional MMT physician shall ensure healthcare staff contacts the previous MMT physician and/or pharmacy to determine the patient's current dose, the date/time of the last dose received to ensure that three or more doses were not missed.
4. The institutional MMT physician shall ensure that protocols to treat a known or suspected opioid overdose are available to all health care staff. NARCAN® must be accessible (i.e. available onsite or via a designated Emergency Room which is in close proximity to the correctional facility).
5. The institutional MMT physician shall make every attempt to educate the patient of potential for relapse and the dangers of overdose, and encourage adherence to treatment.
6. The institutional MMT physician shall not prescribe take-home doses to a patient upon release from the correctional facility.
7. The institutional MMT Physician shall ensure arrangements are made for methadone pick-up at a community pharmacy in the event that a MMT patient/inmate is temporarily transferred from his/her usual correctional facility, whether for an outside pass or for any other reason such as a court appearance.

13.1.2 Guidelines

1. The institutional MMT physician should ensure program rules and expectations are in writing and verbally described to each patient.

2. The institutional MMT physician should ensure dispensing times are clearly defined.
3. The institutional MMT physician should clearly describe the expectations regarding provision of UDS samples, appointments with the MMT physician, and general patient behaviour.
4. The institutional MMT physician should ensure UDS results are maintained in the medical chart.
5. The institutional MMT physician should ensure UDS results are not shared with non-medical staff except when there is a safety issue and that if shared should not be used for punitive purposes.
6. The institutional MMT physician should ensure UDS are performed at intake and periodically thereafter, particularly if the patient shows evidence of intoxication, injection drug use or diversion of methadone.
7. The institutional MMT physician should ensure a process is in place for the safe administration of methadone for patients.
8. The institutional MMT physician should ensure every effort is made to provide continuity of care with a community physician.
9. The institutional MMT physician should ensure a bridging prescription is faxed to a community pharmacy until the patient's next appointment if there is a gap of time from the date of release to the scheduled appointment with the community MMT physician. Details of the prescription should be communicated with the community MMT physician.
10. In the event of an involuntary taper, the institutional MMT physician should ensure counseling and support is provided and that the opportunity for the patient to reapply for MMT is available if they can adhere to program requirements.

13.2 Approaches to Treatment in a Correctional Facility

13.2.1 Approach to Treatment

It must be clear that the interests of the patient are the priority of the institutional MMT physician. A multidisciplinary team approach to the provision of MMT is essential in this setting and should include clinical staff, substance abuse counselors (where available), and persons responsible for the patient's MMT in the community.

Confidentiality is extremely important in the correctional system, as in all medical interactions. Conflicts are often avoidable when the structure of the treatment is conveyed to both patients and staff.

13.2.2 UDS

It is essential that urine toxicology screening results used in MMT correctional facilities is for therapeutic purposes and results should be maintained in the medical chart.

13.2.3 Missed or Vomited Doses

Correctional facilities may have specific procedures in place to handle missed or vomited doses.

13.3 Continuing Ongoing MMT

13.3.1 Issues Unique to Providing MMT in Correctional Facilities

13.3.1.1 Methadone Brought With a Patient

Methadone accompanying any patient should be discarded unless continuity of handling can be proven, such as in a transfer from another correctional facility. (Physicians should refer to the applicable policies of the correctional facility for the discarding of narcotics).

13.3.1.2 Treatment Agreement

The institutional MMT physician shall ensure a treatment agreement is signed by the patient and ensure that the treatment agreement and medical history are kept as part of the medical file.

13.3.1.3 Dosing on Admission

Upon admission to the correctional facility, and prior to dispensing the first methadone dose, confirmation must be obtained that the individual is a community MMT patient.

Often institutional MMT physicians are not available on the weekend to maintain patients on MMT if incarceration occurs after hours, leaving patients at risk for destabilization. For patients who mostly have observed ingestion at the pharmacy with less than or equal to three carries per week, a nurse may assess the patient (vital signs, appearance and level of alertness, symptoms of withdrawal and intoxication and presence of EDDP in their urine) to allow MMT to continue at the same dose. The institutional MMT physician may then fax a methadone prescription to the pharmacy at the correctional facility for the same dose or a lower dose. Alternatively, the patient's community MMT physician may provide a prescription for a bridging dose until the institutional MMT is available, in which case the community MMT physician should consult with the institutional MMT physician to determine the period for which the bridging dose should be prescribed.

In order to provide safe MMT, institutional MMT physicians must use their clinical judgment to determine the appropriate dose (e.g., 50% of the stated dose if diversion of take-home doses is suspected, or of a high maintenance dose, e.g., the dose is greater than or equal to 150 mg). If the dose is reduced, the institutional MMT physician should re-assess the patient frequently for symptoms of withdrawal and intoxication, and appropriate dose changes should be made. Benzodiazepines, or sedating sleep aids should be used cautiously if at all until the institutional MMT physician has done an appropriate assessment of the patient. If the patient appears intoxicated from the nurse's assessment, in these circumstances, the patient should be

assessed within a reasonable amount of time to avoid further discomfort of withdrawal. The Opioid Detoxification Protocol should be followed.

See Section 5.9 Table 09 for protocols on management of missed doses. For patients with "take-home privileges", the physician may wish to verify recent ingestion of methadone by testing for evidence of EDDP in their urine.

13.3.1.4 Dose Increases

In exceptional circumstances due to facility constraints, (e.g., lockdown or offender movement issues) when the institutional MMT physician cannot assess an inmate, the institutional MMT physician should designate a nurse to assess a patient for dose increases. The nurse can give a single dose increase of no more than 10 mg prior to the assessment of the institutional/MMT physician.

The nurse's assessment is documented in the chart and includes the following:

1) The reason why the assessment is being performed by the R.N. and not the physician
2) Any obvious signs of withdrawal noted by the R.N.
3) When the withdrawal symptoms begin in relation to the dose (i.e., 8 hours before the next dose, or 16 hours after the dose)
4) Time of use
5) Drug cravings
6) Time and amount of last dose
7) Mental status
8) Sign and symptoms of sedation
9) Any ongoing opioid use (drug name, amount used, and route of use).

13.4 Observed Administration

It is not uncommon for MMT patients to be under considerable pressure from other patients to divert their medication. Adequate steps to avoid diversion are critical to ensure MMT patients safety within the facility.

Below are suggested recommendations that can be incorporated into the facilities administration process:

- MMT patients to show proper identification.
- MMT patients receiving methadone should be isolated from other patients during administration process.
- Drink water following administration.
- Nurse can inspect mouth before and/or after.
- No wearing of bulky clothing (i.e., parkas, hoodies)
- No bringing cups or containers into the administration area.

- Frisking MMT patients before entering and/or upon leaving administration area.
- Limit access to water post ingestion (fountains, bathrooms).
- A 20-minute direct observation should follow immediately.

13.5 Initiating MMT in a Correctional Facility

If a patient is not receiving methadone at the time of incarceration, the following conditions should be met:

1) The patient must meet or have met in the past the DSM-IV diagnostic criteria for opioid substance dependence.
2) A UDS must be interpreted and a complete assessment performed prior to initiation.
3) The usual reporting procedure to the CPSNL must be followed.
4) Patients not currently using opioids, but where their documented history clearly shows a pattern of long-term opioid dependence continuing until the time of incarceration, should be considered for initiation on methadone while in the correctional facility. (See Section 4 Initial Patient Assessment, Subsection 4.3.4.1 Initial Opioid Positive Urine without Differentiating/Identifying the Specific Opioid).
5) Pregnant patients currently using opioids must be offered MMT while incarcerated (See Section 12 MMT Consideration during Pregnancy).
6) Patients with HIV infection, or hepatitis B or C should be made a high priority for being offered methadone treatment while incarcerated.

13.6 Accidental Overdose of Methadone

Patients should be transported to a community hospital emergency department for assessment and observation. If returned to the institution, a procedure for close observation for at least 24 hours should be in place. Naloxone (Narcan®) must be accessible in all correctional facilities (i.e. available onsite or via a designated Emergency Room which is in close proximity to the correctional facility).

13.7 Out-of-Facility Pass

The institutional MMT physician shall ensure that arrangements are made for methadone pick-up at a community pharmacy in the event of an outside pass or if the MMT patient/inmate is transferred from his/her usual correctional facility for any other reason such as a court appearance.

13.8 Treatment Planning for Release

It is imperative that every attempt to provide good discharge planning is done prior to release. Patients are at highest risk of overdose after release from a correctional facility if an appropriate release plan is not made. However, release dates are not always known and patients may be unexpectedly released precipitously and/or directly from court.

13.8.1 Treatment Planning—Release Date Known

When the release date of the patient is known arrangements should be made in advance. An appointment should be scheduled with the community MMT physician and appropriate clinical information should be sent.

13.8.2 Treatment planning - Release Date Unknown or Unexpected

Patients are often released from custody directly from Court or on very short notice without the knowledge of the facility healthcare staff. Therefore where possible:

1. Patients should receive their daily dose of methadone prior to leaving the facility.
2. Patients should be further advised to contact the facility healthcare staff if they are released directly from court without the benefit of a release plan.

If a patient is released without a community MMT physician, every effort should be made to find one for the patient.

If assistance is required by the facility in finding a local pharmacy that dispenses methadone, contact the Newfoundland and Labrador Pharmacy Board.

13.9 Take-Home Doses

The institutional MMT physician shall not prescribe take-home doses to a patient upon release from the correctional facility

13.10 Involuntary Withdrawal

See Section 8.3

14. Hospital-Based MMT

In many cases, the hospital-based physicians know little about MMT and must rely on the expertise of a MMT physician

14.1 Overview

In many cases, hospital physicians know little about MMT and must rely on the expertise of an experienced MMT physician and/or other hospital professionals with knowledge of methadone – notably pharmacists.

If feasible, the community methadone physician should seek out active hospital privileges so that he or she may write hospital orders for methadone.

Physicians without a methadone exemption are not allowed to order or prescribe methadone unless they receive a special exemption from Health Canada. Temporary exemptions are only valid for one specific patient, and only for the duration of that patient's stay in hospital. Exemptions can be obtained by calling Health Canada, Office of Controlled Substances. In Newfoundland and Labrador, residents are not permitted by the College to prescribe methadone and should not request a methadone exemption.

Hospital physicians, and community methadone physicians with active hospital privileges, should familiarize themselves with hospital policies/procedures in place to accommodate inpatients requiring MMT.

An important aspect of MMT for hospitalized patients is to facilitate the seamless transfer of patients back to their community physician upon hospital discharge.

14.1.1 Standards

None for this section.

14.1.2 Guidelines

1. Attending physicians must be aware of, and follow, hospital policies/procedures in place to accommodate inpatients requiring MMT
2. The attending physician should verify the patient's current dose and date it was last dispensed with the patient's pharmacy.
3. The attending physician should ensure the prescription at the community pharmacy is cancelled for the duration of the patient's hospital stay.
4. The attending physician should conduct a focused assessment with these objectives:
    a. Identify acute risk factors for methadone toxicity.
    b. Obtain a history of methadone use.
    c. Order a UDS if clinically unstable.

d. Order an ECG if patient is on a high dose or has risk factors for arrhythmias.

5. The attending physician's methadone order should specify that the dose is to be mixed in orange juice, and dispensed daily under the observation of a nurse. The order should also specify dispensing dates, and should direct nurses to withhold the dose if the patient shows signs of sedation or intoxication.
6. If the patient is n.p.o., the attending physician may allow the methadone to be mixed in water (or clear juice, with the attending physician's approval).
7. The attending physician should prescribe oral or parenteral opioids to minimize withdrawal symptoms if methadone is not available or is contraindicated (e.g. prolonged QT interval).
8. To avoid methadone toxicity, the attending physician should monitor for the emergence of risk factors during the patient's hospital stay, such as co-prescribing of sedating drugs. The methadone dose should be adjusted accordingly.
9. On discharge, the attending physician may write a prescription for the patient's community pharmacy to last for several days until the patient can see their community MMT physician. A hospital prescription may not be necessary if the patient has take-home doses at home (at the same dose as that provided in hospital).
10. MMT may be initiated in-hospital for pregnant patients, and for patients requiring prolonged hospitalization, who might leave if their acute opioid-withdrawal symptoms are not treated.

14.2 Hospital Pharmacies

Some hospitals may have methadone on their formulary. If methadone is not on the formulary, the patient may bring their take-home doses if available, or a community pharmacy may deliver methadone to the hospital. A take-home bottle should only be used if it is properly labeled and unopened.

14.3 MMT Physicians Working in a Hospital

14.3.1 Verifying the Community Dose

It is not safe to rely solely on the patient's history or the community MMT physician's office for verification of the dose - only the dispensing pharmacist is able to verify with certainty whether the patient has filled their methadone prescription. If the pharmacy is closed and the dose cannot be verified, a safe dose (e.g., 20-30 mg) can be given to ameliorate withdrawal symptoms. If feasible, the urine should be tested to confirm that the patient has recently taken methadone. The attending physician should cancel the methadone prescription for the community pharmacy for the anticipated duration of the hospital stay.

14.3.2 in-Hospital Assessment of the Patient

A focused assessment will identify acute risk factors for methadone toxicity (See Section 4.3.1 Table 04: Patient Factors that Increase Risk of Methadone Toxicity and Section 11: Methadone Toxicity). The following should be included in the assessment:

History:

- Methadone dose, recent changes in dose, missed doses, number of take-home doses per week, and exact date and time of the last dose.
- Recent alcohol and substance use.

Chart review:

- Reason for hospital admission
- Out-patient and in-hospital medications
- Cardiorespiratory, hepatic and renal status.

Investigations:

- Baseline UDS
- ECG if on dose above 120 mg or risk factors for QT prolongation, e.g., electrolyte disturbances.

14.3.3 Hospital Methadone Order

The order should be similar to community prescriptions, specifying that the dose is to be mixed in juice and ingestion is to be observed by a nurse. Start and end dates should be specified in the order and nurses should be instructed to hold the dose if the patient shows signs of sedation or intoxication.

14.3.4 Patients on "Nothing by Mouth" (n.p.o)

If the patient is unable to take oral medications or fluids, withdrawal can be lessened with scheduled doses of parental morphine or hydromorphone. If possible, peripheral and central lines should be avoided in patients who have recently been using injection drugs.

14.3.5 Adjusting the Dose

There have been case reports of serious toxicity in hospitalized patients on methadone, caused by drug interactions or the patient's medical condition. Close monitoring is required if the patient has:

1) medications introduced that are sedating or that inhibit methadone metabolism (See Appendix B: Drug to Drug Interaction)
2) a decreased level of consciousness
3) an acute cardiorespiratory illness
4) missed methadone doses prior to hospitalization
5) has worsening hepatic or renal function.

In these circumstances, frequent observation should be ordered, specifying that the dose is to be withheld if the patient shows signs of sedation or intoxication.

When adjusting the dose the attending physician should keep in mind that acute methadone withdrawal can have serious medical consequences in patients with medical illness. Even

intubated patients in a coma will undergo withdrawal if MMT is abruptly discontinued which can cause agitation and cardiorespiratory instability (Friedman et al. 2003; Kienbaum et al. 1998)**.** Therefore, methadone should not be rapidly tapered or discontinued unless the patient is experiencing methadone-induced intoxication, sedation, or arrhythmias. If it is rapidly tapered, the dose should be carefully readjusted as withdrawal symptoms emerge.

14.3.6 Initiating MMT in Hospital

The treating physician may initiate MMT in hospital for pregnant patients, and for seriously ill patients who require prolonged hospitalization and who might leave against medical advice if their withdrawal is not promptly treated (Aszalos et al. 1999). Vigilance is required, as overdose deaths have occurred even in an inpatient setting.

14.3.7 Opioid Detoxification with Methadone

Inpatient methadone detoxification should only be done by experienced MMT providers in a setting that provides 24-hour nursing and medical coverage. As the patient is closely monitored before and after dosing small p.r.n. doses can be used (e.g., 5 mg q.8.H. no more than 10-15 mg per day). The fixed morning dose can be increased by 10 mg every 2-3 days if the patient requires regular p.r.n. doses. The severity of their withdrawal can be measured using the Clinical Opiate Withdrawal Scale (COWS). Concurrent use of benzodiazepines or other sedating drugs should be avoided.

14.3.8 Discharge from Hospital

If the dose has been adjusted during hospitalization, the attending physician should advise the community MMT physician and the patient should be advised to return the pre-hospitalization take-home doses to the pharmacy.

14.3.9 Exemption from Notice to the College

Attending physicians who are continuing MMT initiated by a community MMT physician are not required to obtain the MMT Program Documentation otherwise required by Section 4.4 of the MMT Standards and Guidelines.

15. Professional Duties and Interprofessional Collaboration

Effective MMT is dependent upon collaboration between physicians and pharmacists, and other health professionals.

15.1 Overview

The MMT Standards and Guidelines identify throughout the need for physicians to communicate and collaborate with other physicians, pharmacists and other health professionals to ensure the safe and effective delivery of MMT.

15.1.1 Standards

Physicians shall use a Physician Pharmacist Treatment Agreement letter (Appendix G).

15.1.2 Guidelines

None for this section.

15.2 Professional Duties

MMT physicians are responsible for the following:

- Provide professional, respectful and reliable services to patients
- Provide back-up coverage for periods when on vacation or otherwise unavailable
- Provide appropriate notice should they close their MMT practice (reference should be made to the College's Guideline – Physician's Responsibilities when Closing his or her Medical Practice for an Extended Period and to the College's Policy – A Physician's Responsibility when Permanently Closing a Medical Practice)
- Assist in the transfer of patients to other MMT physicians (reference should be made to the College's Guideline – Ending the Doctor-Patient Relationship)
- Provide or facilitate patient access to health and social services, such as primary health care
- Remain current in practices and standards for MMT and the treatment of opioid dependence
- Communicating and collaborating with pharmacists and other care providers for the benefit of the patient.

15.3 Interprofessional Collaboration

15.3.1 Physician-Pharmacist Collaboration and Communication

Many problems in patient care have been found to be a direct result of lack of communication between MMT prescriber and pharmacist (CAMH, November 24, 2010). To optimize patient care, communication between physicians and pharmacists is essential in the following circumstances:

- Determining at the outset of treatment whether a pharmacy is accepting new patients

- Ensuring that both the MMT prescriber and the pharmacist are accessible and cooperative in their communications with each other
- Developing means for the pharmacist to reach the MMT prescriber for urgent issues after hours
- Relaying to each other pertinent clinical information (e.g. pregnancy), missed doses, vomited doses, and where appropriate confirming follow-up measures

The pharmacist and the physician play an important role in MMT. Collaboration and regular communication between pharmacists and MMT prescribers can have a positive impact on patient care and safety (OCP, September 2010).

15.3.2 Physician Pharmacist Treatment Agreement Letters

It is a standard that physicians use a Physician Pharmacist Treatment Agreement Letter. (See Appendix G: Physician Pharmacist Treatment Agreement Letter.)

16. Application of New MMT Standards and Guidelines

The new MMT Standards and Guidelines will apply to both new and existing MMT patients.

16.1 Overview

The new MMT Standards and Guidelines apply to the practices of MMT physicians for all of their MMT patients, including on a go-forward basis to those patients who were receiving MMT prior to the effective date of the new MMT Standards and Guidelines.

The effective date of the new MMT Standards and Guidelines is May 1, 2013.

16.1.1 Standards

1. Application of new MMT Standards and Guidelines to new MMT patients

Patients being assessed for initiation of MMT on or after the **Effective Date** of the new MMT Standards and Guidelines shall, from the outset, be assessed and treated by the MMT physician in accordance with the new MMT Standards and Guidelines.

2. Application of new MMT Standards and Guidelines to existing MMT patients

With respect to patients who were already receiving MMT prior to the **Effective Date** of the new MMT Standards and Guidelines, MMT physicians shall take the following steps

A. Within **90 days** of the **Effective Date**, the MMT physician shall **assess** whether the current MMT treatment of that patient is in **compliance with** the **new MMT Standards and Guidelines**;

B. If the **current MMT** of that patient is **not in compliance** with the new MMT Standards and Guidelines, the MMT physician shall **bring the MMT** of that patient **into full compliance** with the new MMT Standards and Guidelines **within 90 days of the assessment** referred to in Step A above. Bringing the MMT of that patient into compliance with the new MMT Standards and Guidelines will include

i. the signing by that patient of the Treatment Agreement required by the new MMT Standards and Guidelines (Appendix D);

ii. application of the new Dosage and UDS Standards and Guidelines for the applicable stage (early stabilization, late stabilization or maintenance) of the patient's MMT;

iii. application of the new Take-home doses Standards and Guidelines; and

iv. application of those other MMT Standards and Guidelines as applicable to the patient.

C. **MMT physicians must suspend MMT** (in accordance with the Involuntary Withdrawal protocol set out in Section 8 of this document) to a patient if, following Steps A and B under Standard 16.1 (2) above, the MMT physician believes that a continuing variation between the MMT and the MMT Standards and Guidelines raises a risk to the MMT patient or to the public. For example, any of the following variations from the MMT Standards and Guidelines should be considered as grounds for suspension of MMT:

- the refusal of the patient to sign the Treatment Agreement
- the refusal of patient to provide UDS samples in accordance with the UDS Standards and Guidelines
- the refusal of the patient to use a locked box for the home storage of take-home doses

D. **If the MMT physician believes there are exceptional circumstances** which may justify an extension of the time period set out in Step A or Step B of this Standard, either for their practice as a whole or for a particular MMT patient, the MMT physician must request approval from the College for such an extension.

3. **MMT physicians must, for both new and existing MMT patients**, complete the Appendix T: Checklist, as a record of their implementation of the MMT Standards and Guidelines. MMT physicians must, on request of the College, provide a copy of the completed Checklist for each of their MMT patients.

4. **MMT physicians must document any variation** from the MMT Standards and Guidelines, in accordance with the College's definitions of "Standards" and "Guidelines" set out in sections 1.1.1 and 1.1.2 of this document.

16.1.2 Guidelines

None for this section.

Appendix A: Diagnostic Criteria for Substance Dependence:

Reprinted with permission from the Diagnostic and Statistical Manual of Mental Disorders, Text Revision, Copyright 2000, American Psychiatric Association.

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. the need for markedly increased amounts of the substance to achieve intoxication or the desired effect;
    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);
    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 physicians 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 worsened by alcohol consumption).

Specify if:

With Physiological Dependence: evidence of tolerance or withdrawal (e.g., either Item 1 or 2 is present).

Without Physiological Dependence: no evidence of tolerance or withdrawal (e.g., neither Item 1 nor 2 is present).

Appendix B: Drug to Drug Interactions

Physicians need to be aware of common methadone-drug interactions. Many of these interactions involve the cytochrome P450 (CYP450) enzymes. While there are more than 28 CYP enzymes (Flexner and Piscitelli 2000; Shannon 1997; Wilkinson 2005, as cited in Levitt, 2005) the most important enzymes in methadone metabolism are CYP3A4 and CYP2B6. As Levitt (2005) points out, some P450 interactions may be potential (i.e. theoretical), others are currently being investigated to confirm their clinical significance.

Of importance to physicians is how the substances that interact with the CYP450 system work to increase or decrease the level of methadone. Substances may act as substrates, inhibitors or inducers, as outlined below:

> **Substrate** -Any drug metabolized by one or more CYP enzymes
> **Inhibitor** - Any drug that slows the metabolism of drugs that are substrates, which may result in excessively high drug levels
> **Inducer** - Boosts the activity of specific CYP enzymes resulting in more rapid metabolism of substrate drugs, which may result in lower than expected levels of substrate drugs.

Pharmacodynamic

Additive effects of:

- Another central nervous system (CNS) depressants, e.g., alcohol, benzodiazepines, other sedating medications e.g. dimenhydrinate, clonidine, when combined with methadone
  - High risk patients for toxicity on initiation
  - Risk of CNS depression during treatment.
- Medications causing similar effects e.g., constipation or urinary retention by anticholinergics.
- Medications causing prolongation of QTc interval e.g., tricyclic antidepressants, cocaine (see http://www.azcert.org/medical-pros/drug-lists/printable-drug-list.cfm and other websites).

Pharmacokinetic

Methadone is metabolized by several CYPs, predominantly by 3A4 enzyme system and to a lesser extent CYP 2B6, 2D6 and 1A2. Others may also be involved.

Important Considerations in Methadone Interactions

Some important considerations in methadone interactions are noted in the table below:

With Medications that are 3A4 Inhibitors	With Medications that are 3A4 Inducers
Fast onset	Slower onset
Possible increase in methadone effects including toxicity and overdose	Can result in decreased methadone effects and withdrawal symptoms
Extra care required during initiation of methadone	

Clinicians should take special care when medications are started or discontinued.

The following websites may be consulted:

- http://www.atforum.com/SiteRoot/pages/addiction_resources/Drug_Interactions.pdf
- http://www.hivclinic.ca/main/drugs_home.html

Appendix C: Initial Patient Assessment Form

INITIAL PATIENT ASSESSMENT FORM

Please complete the following questionnaire as accurately and honestly as possible so that we can determine what kind of treatment would serve you best.

NAME (Last, First Middle):

DATE OF BIRTH (M/D/Y): GENDER (Please Circle) - MALE / FEMALE

ADDRESS (Residence and Mail):

PHONE NUMBERS – HOME ( ) WORK ( ) CELL ( )

A PERSON TO CONTACT IN CASE OF EMERGENCY (STATE RELATIONSHIP, E.G. SPOUSE, PARENT, SIBLING):

CONTACT'S PHONE NUMBER - ( )

DRUG HISTORY

	Amount Used	How Often	First Used	Last Used
Heroin				
Other Narcotics				
Cocaine				
Barbiturates				
Amphetamines				
Cannabis (Pot, Hash)				
Benzodiazepines (Valium, Ativan)				
Cigarettes (Packs Per Day)				
Alcohol				

Are you taking any prescribed medications? If yes, please provide details including type and amount.

Are you now or have you ever been prescribed narcotics (e.g., Tylenol #3, Percodan, Percocet, Dilaudid, Talwin, morphine) for an extended period of time (e.g., for more than four weeks)? If yes, please provide details below.

Type:

Amount prescribed (per week or month):

For how long? (Weeks/Months/Years):

For what reason was it prescribed?

If it has been discontinued, when and why?

Do you have any drug allergies or are there medications you cannot take? If yes, please provide details.

PAST MEDICAL HISTORY

Condition	*Please Check Most Appropriate Test Result*				**Comments** *(Dates and locations of tests, etc)*
	Negative	**Positive**	**Don't Know**	**Never Tested**	
Hepatitis A					
Hepatitis B					
Hepatitis C					
HIV					
Tuberculosis Skin Test					

	YES	***NO***		***YES***	***NO***
Do you suffer from migraines?			Do you have ulcers?		
Do you have back problems?			Do you have heart problems		
Have ever overdosed?			Have you been in a car accident?		
Do you have Asthma?			Do you suffer from seizures?		
Have you ever done I.V. drugs?			Are you presently an I.V. drug user?		
Have you ever shared an I.V. needle?			Is your doctor aware of your drug issue?		

What operations have you had (please give type and year)? Do you have any other medical issues?	**Please provide the name and address of your family doctor.**

WOMEN ONLY

When was the first day of your last menstrual period?

What is your current method of contraception? The Pill/condoms/other:

Is there any chance you might be pregnant? Yes / No

EMOTIONAL HEALTH

Have you been treated by a family doctor or psychiatrist for: Anxiety -Yes/No Depression - Yes / No

Have you been admitted to a psychiatric facility? Yes / No

Have you received treatment for any other emotional problems? Yes / No

Have you suffered abuse? (mental, sexual or physical) Yes / No

Have you ever attempted suicide? Yes / No

Are you currently depressed or suicidal? Yes / No

FAMILY HISTORY

Does your family have a history of medical problems like alcohol or drug abuse, depression, heart disease, etc.?

DRUG TREATMENT PROGRAMS:

Please provide details of any drug treatment programs attempted - include detox attempts, program name, when, how long did you stay clean/why failed?

SOCIAL HISTORY

Are you: married/single/separated/divorced/common-law/widowed

Do you have children? Yes/No Are the children in your custody? Yes / No

Who lives in your household?

Do they abuse alcohol/drugs? Yes / No

Are the people close to you aware of your drug problem? Yes / No

What is your occupation? Are you currently employed? Yes / No

Last job held: (Dates - from when to)

What is your highest level of education?

Are you receiving: Income Support/family allowance or other government child benefits/pension/UI/none/other?

Do you drive a car? Yes / No

LEGAL STATUS

Are you currently on probation or parole? Yes / No - If yes, until when?

Is treatment a condition of your probation? Yes/No - If yes, when?

Do you have any Court dates pending? Yes/No - If yes, when?

Do you have previous convictions? Yes/No - If yes, for what?

Have you been incarcerated? Yes/No - If yes, for what?

How long have you been in jail for in total?

Have you been charged with impaired driving? Yes/No

Have you been charged with a crime that included a weapon or violence? Yes/No

ABOUT YOUR ADDICTION

In the last 12 months:

Do you need more and more of the drug you are using to get the same effect? Yes / No

Describe what symptoms you experience if you suddenly stop taking the drug:

Do you frequently take more drugs than you planned, or use it for longer than you planned to? Yes/No

Have you had many unsuccessful attempts to cut down on your drug use? Yes/No

Do you spend a lot of your day getting, using, and recovering from the effects of drugs? Yes/No

Have you given up work, social or other things you used to do because of your drug use? Yes/No

Do you keep taking drugs, despite the harm and problems it is causing you? Yes/No

Why have you come for treatment at this time?

What type of treatment do you feel that you need?

What are your goals for treatment?

PATIENT SIGNATURE: **DATE:**

Appendix D: Methadone Maintenance Treatment Agreement

Note to physicians: It is important that the patient receive clear information about the MMT program rules and expectations. Policies on take-home doses, urine drug screens, appointments, and treatment withdrawal should be specified. The MMT physician should provide a copy of the treatment agreement to the patient and revisit it once the patient is stabilized.

Methadone Maintenance Treatment Agreement

There are provincial rules that must be followed by doctors who prescribe methadone and pharmacists that dispense it. This agreement has been prepared to both tell you about methadone maintenance therapy, as well as to make a record that you agree to the rules.

Things you need to know about methadone and the methadone program

To get into the methadone program, you have to sign your name on the last page. When you sign your name, it means you understand the things below. If you don't understand these things, ask your doctor to explain them to you. If you still don't understand these things after talking to your doctor, you should not sign your name on the last page.

1. The kind of drug you are trying to quit is called an opioid. (Opioids are drugs like heroin, Dilaudid, codeine, morphine, and Percocet).
2. You have tried hard to quit taking this drug but you still can't stop.
3. You are dependent on the drug you are trying to quit. (Dependent means that if you don't get the drug, you usually feel really bad or get sick).
4. You are going to be given a drug called methadone to help you quit taking the drugs you are dependent on.
5. Methadone is an opioid drug, but it is different because it can help you stop taking the other opioid drug you are dependent on.
6. If you suddenly stop taking methadone, or take less of it, you will probably feel very sick.
7. You are expected to tell your methadone doctor all of the drugs you take, even if they are prescription drugs that are prescribed for you.
8. While you are taking methadone, you could get very sick or die if you take any drugs that change your mood. Some drugs that could change your mood are opioid pain killers (such as Dilaudid, morphine or Oxycontin/OxyNeo), alcohol, cocaine, heroin, sleeping pills, or tranquilizers (pills that relax you, like benzodiazepines).
9. You can leave the methadone treatment program whenever you want.
10. If you are pregnant or if you get pregnant, you know that your baby will become physically dependent on methadone and, once born, may suffer opioid withdrawal that requires specialized care and opioid replacement therapy.
11. You should not eat poppy seeds when you are taking methadone because they might make it look like you are taking opioid drugs if you have a urine (pee) test.
12. Some drugs you can buy in a drugstore without a prescription could make it look like you are taking opioid drugs if you have a urine (pee) test. You should ask the pharmacist if any drug you buy without a prescription (even cough syrup) might affect a urine test for opioids.
13. When you take methadone, there might be some changes to the way you feel. You might sweat more, you might not be able to move your bowels (poop) as easily as before, you might

lose interest in having sex, you might feel different when you have sex, you might feel tired, you might put on weight, and you might urinate (pee) less. These changes will probably not be too bad, but your methadone doctor can help you if they happen. If you take the methadone the way your methadone doctor tells you to, the methadone probably won't give you any more problems than that.

14. If your methadone doctor thinks that the methadone is not working for you, the methadone doctor may stop giving you methadone, or give you less.
15. If you seem drunk or high, or if you act strangely, you may be asked to see a doctor, and you may be given less methadone or none at all.

Things you are expected to do

1. When you sign your name on the last page, it means you know you are expected to do the things below. If you don't do these things you may have to leave the program. If you don't understand these things, ask your methadone doctor to explain them to you.
2. If another doctor or dentist gives you a prescription or offers to give you a prescription, you are expected to tell them you take methadone.
3. You are expected to tell the methadone doctor whenever you have been given a prescription from any other doctor or dentist. You know that if you don't tell the methadone doctor about getting a prescription for another pain-killer, you could be charged with a crime called double-doctoring.
4. You are expected not to drive or operate machines when you start taking methadone and when your methadone doctor changes your dose of methadone. Your methadone doctor will tell you when it is OK to start driving or using machines again.
5. You are expected to take only one dose of methadone a day. When you have to take the methadone at the methadone clinic or pharmacy, you are expected to let a clinic or pharmacy staff member watch you take it.
6. You are expected to tell any other doctor or dentist you see that you take methadone. When you see Dr._____, you are expected to bring your prescriptions or drug containers.
7. Whenever your methadone doctor or the methadone clinic or pharmacy staff say so, you are expected to give a urine (pee) sample that will be tested for drugs. If you don't give a sample, the methadone clinic or pharmacy may give you fewer take-home doses of methadone, or it might not let you take methadone home at all.
8. If you do anything with your urine (pee) sample to make it seem like you are not taking drugs, or if you try to pass off someone else's urine (pee) sample as your own, the methadone clinic or pharmacy may give you fewer take-home doses of methadone, or it might not let you take methadone home at all.
9. You understand that you should take drug counseling while you are in the methadone program.
10. You agree to keep all your appointments with the doctor who is prescribing methadone for you. If you miss appointments, your methadone doctor may prescribe fewer take-home doses of methadone, or it might not let you take methadone home at all.
11. If you are given take-home doses, you will have to store your methadone securely in a locked box.

Things you are not allowed to do

When you sign your name on the last page, it means you know that you are not allowed to do the things below. If you do these things, the methadone clinic or pharmacy may not give you methadone. If you don't understand these things, ask your methadone doctor to explain them to you.

You are not allowed to:
1. Arrive late, after the clinic or pharmacy hours
2. Hurt or threaten to hurt the staff or other patients
3. Don't show proper ID, such as a drivers' license, when you are asked to
4. Miss three or more doses of methadone in a row
5. Take a dose of methadone less than 16 hours before your next dose

When you sign your name on the last page, it means you know that you are not allowed do the things below. If you do these things, you may have to leave the methadone program. If you don't understand these things, ask your doctor to explain them to you.

You are not allowed to:
1. Hurt or threaten to hurt the staff or other patients
2. Carry any kind of weapon, including a knife or a gun
3. Sell or use drugs in or near your methadone doctor's office or clinic, or in or near your pharmacy, or do anything else that is illegal
4. Never give or sell your methadone to others
5. Shout, swear, fight or argue in or near your methadone doctor's office or clinic or in or near your pharmacy
6. Ask people for money in or near your methadone doctor's office or clinic, or in or near your pharmacy
7. Break, damage, or steal anything in or near your methadone doctor's clinic, or in or near your pharmacy
8. Insult or make fun of people because of their sex or skin colour, or because of the way they behave or look

Consents

When you sign your name on the last page, it means that you will let your methadone doctor, and other health workers involved in your methadone treatment, do the following things:

1. Let your methadone doctor give the College of Physicians and Surgeons of Newfoundland and Labrador your name, date of birth, MCP number, address, and the date you started taking methadone, and other information that may be required by the College.
2. Let your methadone doctor talk to other doctors or health workers about your care.
3. Let your methadone doctor, your pharmacist and other health workers involved in your methadone treatment talk to other pharmacists or other health workers to check on how much methadone you were given at another place.
4. Let your methadone doctor and pharmacist discuss and agree on conditions for your receiving methadone from the pharmacy.

Confidentiality

Everything you tell the methadone doctor's office or clinic staff will be kept private, unless someone who works at the office or clinic thinks that:

1. A child is being harmed or not taken care of. There is a law that makes the clinic tell this to the social services department.
2. You might kill yourself, kill someone else, or if you can't take care of yourself. If this happens, you may have to see a psychiatrist, even if you don't want to.
3. You may hurt someone. Under the law, your methadone doctor may tell this to the police department.
4. You should not be allowed to drive because you are high, drunk, or for some other reason. There is a law that makes the clinic tell this to the driving license department.
5. You have AIDS, HIV, Hepatitis B or Hepatitis C, and some other diseases. There is a law that makes your doctor tell this to the health department.

When you sign your name on the last page, it means that you:

1. Will not tell anyone (even your family or friends) the names of the other patients at the methadone clinic or pharmacy, or anything else about the patients.
2. Have talked to the methadone doctor about this agreement. If you don't understand these things after talking to your doctor, you should not sign your name.

3. Agree that if you don't do what this agreement says, you may have to leave the methadone program.

_____

Patient's Signature

_____

Patient's Name (Print)

_____

Dated (dd/mm/yyyy)

_____

Doctor's Signature

_____

Doctor's Name (Print)

_____

Dated (dd/mm/yyyy)

Appendix E: Patient Initiation/Continuation to MMT Form – No Longer Required

Appendix F: Sample Methadone Prescriptions

Prescriptions for methadone in Newfoundland and Labrador must be written on the Tamper Resistant Prescription Pad (TRPP). For more information on the TRPP program, visit the CPSNL website (https://www.cpsnl.ca/default.asp?com=PracticeAd&m=371&y=2010&id=9) or the Department of Health and Community Services website (http://www.health.gov.nl.ca/health/prescription/hcp_tamperresistantdrugpad.html).

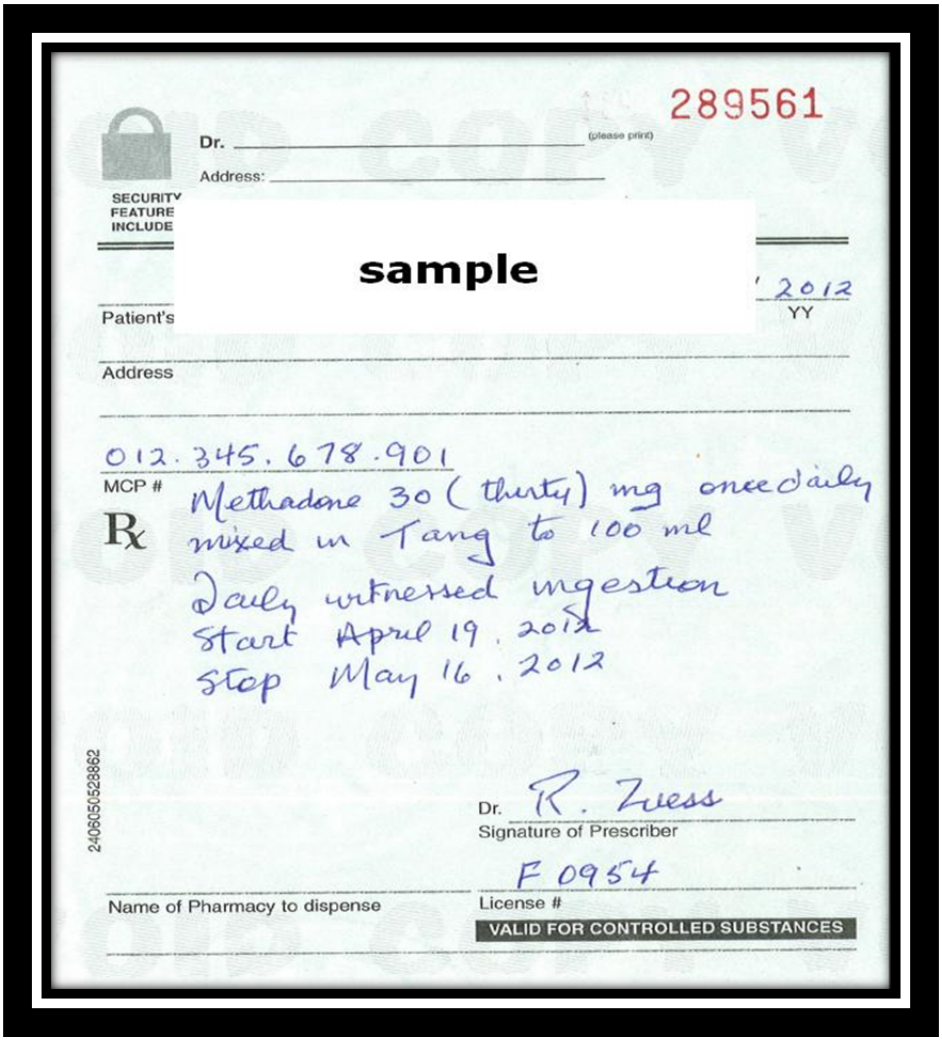
The methadone maintenance therapy physician must specify:

1. **The total quantity in milligrams, written in numbers and words to help to prevent tampering of prescriptions**.
2. **The daily dose mixed in Orange Tang or other crystalline juice. The standard final volume is 100 ml**. Patients unable to tolerate 100 ml of juice can have the methadone mixed to a final volume of 50 ml. Patients who are under NPO orders can have methadone mixed to a final volume of 15 ml. For doses mixed to a final dose other than 100 ml, the physician should communicate with the pharmacist.
3. **The days of the week that require witnessed ingestion**.
4. **The number take-home doses (carries) per week and days of week that are to be given as take-home doses, if applicable.**
5. **The start and end date.**

Two samples follow to illustrate a prescription at a stable dose and a prescription with a take-home dose.

1. Prescription at a stable dose:

This prescription represents a stable dose of methadone with daily witnessed dispensing.



2. Prescription with a take-home dose:

This prescription represents a stable dose of methadone with one weekly take-home dispensing.

The prescription must clearly state the days on which the patient is to visit the pharmacy to receive a witnessed dose and the number of take-home doses per week.

Appendix G: Physician-Pharmacist Treatment Agreement Letter

Doctor's Name and Clinic
Address
Telephone
Facsimile

Dear Pharmacist,

Our patient has requested to attend your pharmacy for Methadone Maintenance Treatment. We encourage an active communication between pharmacist and physician.

I have already discussed the following safety measures, methadone dispensing practices, and clinic policies with the patient. Please feel free to contact me to discuss any of these matters or any further suggestions that your team may have for this patient's clinical care.

You may call/page me at _____. (PLEASE DO NOT GIVE THIS PAGER/PHONE NUMBER TO THE PATIENT.)

- Patients are required to drink methadone dispensed in approximately 100 ml orange Tang or other crystalline juice in front of the pharmacist. You or a member of your team must witness ingestion of methadone every day for patients receiving daily dispensing and on the day that patients pick up their doses for patients receiving take-home doses. Ask the patient to speak after their drink to ensure that has been swallowed.

- The pharmacy team shall inform the methadone physician of any information or observed evidence of diversion of methadone.

- The pharmacist shall inform the methadone physician of missed methadone doses by the patient.

- If the patient misses three (3) or more doses in a row, withhold the methadone dose from the patient to prevent an overdose. The methadone physician must reassess the patient before methadone is restarted.

- If there is any evidence of intoxication, sedation or impairment (slurred speech, stumbling gait, disorientation), the pharmacist must withhold the methadone dose from the patient to prevent a possible overdose. The pharmacy team must contact the methadone physician to inform them of the observation of concern. If the patient returns within eight (8) hours of their originally scheduled, witnessed ingestion, and the pharmacist is satisfied that the patient is no longer intoxicated, sedated or impaired, the pharmacist may give the patient the withheld dose. However, the pharmacist may not release any take-home doses until reauthorized by the physician.

- If the pharmacist observes evidence of an overdose, he or she must advise the patient to receive urgent medical care. The pharmacist may call 911 for transport to hospital. The

pharmacist will contact the physician directly to inform them of the overdose and treatment directives.

- Dispense take-home doses in childproof bottles. Patients are advised to store any take-home doses in a locked metal box to ensure community safety (i.e., to avoid misplacement/loss and consumption of methadone by someone other than to whom it is prescribed). The pharmacist may request that the patient present the locked box prior to issuing take-home doses.

- Pharmacists may replace any doses of methadone vomited only if the pharmacist or a member of the pharmacy team has witnessed the vomiting within 30 minutes of ingestion. The replacement dose should be no more than 50% of the original vomited dose. The pharmacist should inform the methadone provider regarding the vomited dose.

- The start and end date recorded on the prescription are the first day and the last day the patient is authorized to receive a dose for that prescription. The pharmacist must not dispense any methadone from that prescription after the end date, regardless of the fact that there may be doses remaining on that prescription.

- The physician may authorize a patient to receive take-home doses based on their clinical stability. Providing take-home doses to a patient before they are clinically stable puts them and the public at risk of overdose and diversion. Providing take-home doses for patients because the pharmacy is closed is a last resort when all other steps outlined in the *NLPB MMT Standards of Practice* and the *CPSNL Methadone Maintenance Treatment Handbook* have been exhausted, and then only in accordance with these documents.

  (Note: Physician and pharmacist may agree on additional terms, provided they are not contrary to the CPSNL MMT Standards and Guidelines).

Sincerely,

/signature/

Name of Physician
CPSNL License Number

Name: _____

Date: _____

Current Methadone Dose: _____mg

Number of Take-home Doses: _____

Missed doses: Yes – No _____

Supervised UDS:

Methadone: _____
Cocaine: _____
Opiates: _____
Benzodiazepines: _____
Oxycodone: _____
Creatinine: Normal/Abnormal
Interpretation of UDS _____

Patient stated drug/alcohol use and route

Since last visit:

Opiates: Yes – No _____
Cocaine: Yes – No _____

Benzodiazepines: Yes – No _____
Alcohol: Yes – No _____

Other problematic drug use: Yes – No _____

Opioid Cravings:

None – Mild – Moderate – Severe

Psychological Issues Update

Mood: Normal - Other

Sleep: Normal - Insomnia
Anxiety: Absent - Present

Energy: Normal – Other _____

Suicidal Ideation: Absent - Present - NA

O/E:

Appearance: Alert – Intoxicated
Behaviour: Normal – Abnormal
Gait: Normal – Abnormal
Speech: Normal – Abnormal
Eye contact: Normal – Abnormal

Reported methadone sedation: Yes – No

Reported methadone withdrawal: Yes – No

Take-home dose safety issues discussed: Yes – No – NA

Reviewed dangers of methadone diversion: Yes – No – NA

Clinically stable: Yes – No

Take-home doses locked up in a box: Yes – No – NA

Opioid Withdrawal:

None – Mild – Moderate – Severe

Safe with take-home doses: Yes – No

Opiate Withdrawal Symptoms:

None – Insomnia – Anxiety – Dysphoria – Nausea - Diarrhea - Hot flashes – Irritably
Myalgia - Restlessness – Rhinorrhea – Sneezing – Sweats - Yawning - Pupil dilated – Malaise – Abdominal Cramping – Piloerection

Stable housing: Yes – No

Stable employment/social spt: Yes – No

Timing of Withdrawal from Last Dose:

Reported methadone withdrawal: Yes – No

Counseling/Clinical Notes:

_____

_____

_____

_____

Plan:

Rx: Methadone _____ mg po od from _____ to _____

Take-home doses: M T W T F S S for _____ week (s) RTC _____day/week

Appendix I: Managing Potential Methadone Overdose

This appendix includes documents to assist physicians in handling a potential methadone overdose. These materials are also intended to provide advice to patients and emergency room staff, and ensure that physicians who prescribe methadone have taken the necessary steps to avoid an adverse outcome in a methadone overdose scenario. (See Appendix J: Patients Guide on methadone overdose)

Reducing Risk of Toxicity During Initiation and Early Stabilization

Patient education

- The patient is to limit driving or use of machinery after a dose increase, particularly in the first few hours after dosing.
- The patient is to take the methadone dose in the morning, since the risk of overdose is increased at night.
- Whenever feasible (with the patient's consent), a family member or significant other should be educated about the symptoms of toxicity with instructions to go to the emergency department immediately at the first sign of toxicity. A patient information guide may be used for this purpose

Explain the risks of diverted methadone

- A single dose of methadone can be fatal.
- Patients are responsible for the safe storage of their methadone (See Appendix L: Take-Home Dose Agreement).

Frequency of visits

- The MMT physician shall see the patient at least every one to two weeks.
- Twice-weekly visits during the first two weeks of treatment are recommended, particularly if the patient is at increased risk for methadone toxicity or cannot be stabilized at a low dose. If possible, the visits should be scheduled for two to six hours after the methadone dose. The MMT physician should inquire about sedation and other side effects.

Take-home doses

- No take-home doses shall be granted during the first three months of treatment, unless there are extraordinary circumstances in accordance with Section 7: Take-Home Doses.

Avoid prescribing any sedating drugs

- Includes benzodiazepines, non-benzodiazepine hypnotics, antipsychotics, antidepressants, and sedating antihistamines. Even moderate, therapeutic doses of these drugs may increase the risk of toxicity if they are initiated at the same time as methadone and the patient is not fully tolerant to their sedating effects.
- Patients should also be advised to avoid alcohol and over-the-counter sedating drugs.

Tapering High-dose benzodiazepine user

- Benzodiazepine abuse and dependence are common in this population.
- As with opioids, it is difficult to judge a patient's benzodiazepine use and tolerance accurately.
- Benzodiazepine tapering, while difficult on its own, can be very complicated and potentially unsafe when attempted with MMT initiation.

Intoxication or sedation

- At any stage of MMT, the pharmacist should be instructed to alert the MMT physician if the patient appears sedated or intoxicated.
- Intoxicated patients should not be medicated until assessed by their MMT physician.
- If signs of intoxication are observed after ingestion of methadone, the patient should be sent to the hospital by ambulance for assessment.

Appendix J: Patient Guide on Methadone Overdose

These are important things you need to know about methadone. If you do not understand these things, ask your methadone doctor or someone at your methadone doctor's office or clinic.

You should always (and only) take the amount of methadone that your methadone doctor prescribes for you. No more and no less. Taking too much of a drug is called an overdose. An overdose of methadone can make you very sick and might even kill you.

If you are new to methadone or if you have not been taking your regular dose, even for a few days, **you are at increased risk of overdose**.

If you take too much methadone you may have trouble breathing, you may get tired, or the black circles in the middle of your eyes (pupils) may get very small. If this happens, you should let your methadone doctor or someone at your methadone doctor's office or clinic know right away. If you cannot reach your methadone doctor's office or clinic, you should call an ambulance or go to the emergency room.

Doctors can do things to make you better if you take too much methadone.

Even if you have been on methadone for a long time, taking more methadone than you are supposed to take can be dangerous. Even a little bit more methadone could make you very sick and might even kill you.

Your nurse, pharmacist or doctor may tell you that **IT IS ESSENTIAL THAT YOU GO TO THE EMERGENCY DEPARTMENT** to be observed. You may need to be observed for 10 hours, and maybe longer, depending on your symptoms.

There is good treatment available in the emergency department that can make you feel better if you take too much methadone.

Below are some questions that people who take methadone often ask. You should read these and make sure that your family or the people you live with also read them. If you don't understand any of these things, ask your methadone doctor or someone at your methadone doctor's office or clinic.

Why can't my doctor increase my dose more quickly?

Because your body takes time to get used to methadone, your doctor has to go slowly, and not give you too much methadone to begin with. Most drugs don't build up slowly in your body like methadone does. If you got a full dose of methadone right away, you would probably get very sick and might even die. A dose of methadone that might feel like too little on a Monday could put you in hospital by Thursday.

What can I do to feel better when I stop taking the drugs I used to take, and I go through withdrawal? What if I can't sleep?

Taking a drug that your doctor doesn't know about could make you very sick or even kill you. Always ask your doctor what you can take while you are on methadone. You doctor will know about things that can make you feel better that won't make you sick.

Prescription pain killers, alcohol, allergy pills, cocaine, crack, heroin, sleeping pills, or tranquilizers (pills that relax you, like benzodiazepines) can be very dangerous if used with methadone.

Isn't methadone supposed to make you sleepy?

No. You are supposed to feel normal on methadone, not high or sleepy. Methadone builds up slowly in your body so feeling sleepy during the day may not happen until several days after you have been given a bigger dose. If you start to feel sleepy during the day, you should let your methadone doctor know right away, because this could be a sign of overdose.

How do I know if my methadone dose is too high?

- You may feel sleepy, and nod off several times during the day.
- You may be forgetful.
- You may be difficult to wake up from your sleep.
- You may have slurred speech, stumble, or seem drunk.

If any of these things happen, you should let your methadone doctor's office or clinic know right away. If you can't reach your methadone doctor's office or clinic, you should call an ambulance or go to the emergency room.

What can I do to make sure I don't overdose?

- Only take your methadone in the morning.
- See your methadone doctor or nurse twice a week for the first two weeks.
- Don't take prescription pain killers, alcohol, allergy pills, cocaine, crack, heroin, sleeping pills, or tranquilizers (pills that relax you, like benzodiazepines).
- Tell your family and close friends that you are on methadone.
- If they see that you're drowsy, tell them they must call your methadone doctor or an ambulance.

I've been offered a small amount of methadone by another patient at the pharmacy. This can't hurt — I know I need 80 mg and I'm only at 45 mg.

Never take extra methadone. It's probably safe for your friend, but it could kill you. You took 80 mg **once** and were okay. If you had taken 80 mg every day for three or four days, you might have died. Remember, it takes five days for the dose to build up in your blood.

I get take-home doses. If I have a friend who goes into withdrawal, is it safe to give him a little bit of methadone?

No it isn’t safe, because your friend is not used to methadone. A dose that is just right for you could kill your friend.

Appendix K: Opioid Withdrawal and Tolerance

Physicians titrating methadone must be familiar with the clinical features of opioid withdrawal.

Opioid Withdrawal

Opioid withdrawal peaks at 2–3 days after the last use. Physical symptoms largely resolve by 5–10 days, although psychological symptoms can continue for weeks or months.

Serious complications of withdrawal include miscarriage, premature labour, suicide, and overdose or relapse due to loss of tolerance.

Opioid Withdrawal Signs and Symptoms

Physical Symptoms	Psychological Symptoms	Physical Signs
Myalgia Abdominal cramps Nausea Chills Hot flashes Electric or uncomfortable feeling Yawning	Restlessness Dysphoria Insomnia Anxiety Irritability Fatigue Drug craving (the insomnia and anxiety may be severe and distressing)	Lacrimation Rhinorrhea Dilated pupils Abdominal tenderness Vomiting Diarrhea Sweating Chills Piloerection Tachycardia Hypertension

The patient on inadequate doses of methadone will describe a characteristic set of symptoms. The symptoms appear a certain number of hours after the methadone dose, although there may be some variation with the patient's activity level and other factors. The onset of symptoms is delayed with each dose increase.

Alternative explanations should be sought if the patient:

- gives an inconsistent history of withdrawal symptoms;
- has one isolated symptom (such as insomnia or nausea);
- advises the onset of symptoms is not related to the time of the dose; or
- has been taking a stable dose and suddenly complains of withdrawal (see below).

A dose might be considered acceptable if the patient sleeps comfortably at night and only has mild withdrawal symptoms on awakening, which are tolerable to the patient.

Conditions Commonly Confused with Withdrawal

The clinician should determine why the patient continues to report withdrawal symptoms despite dosage adjustment. Common reasons for ongoing withdrawal include:

- medication use that speeds methadone metabolism (such as phenytoin, chronic alcohol use)
- opioid use
- diverting doses

Physicians should consider a medication review with the pharmacist. The following conditions cause symptoms that are confused with withdrawal.

Pseudonormalization should be suspected if the patient regularly complains some weeks after a dose increase that it is no longer 'working.' Patients who are mildly intoxicated on opioids feel more enthusiastic and energetic. As they develop tolerance, they may feel they need a dose increase to recreate this effect, which they view as both desirable and normal.

Insomnia is often the dominant symptom of opioid withdrawal. Other causes should be ruled out if the patient reports insomnia that isn't accompanied by other withdrawal symptoms and is not relieved by a dose increase. Depression, anxiety, and use of alcohol and cocaine are common causes of insomnia in this population. A careful sleep history will identify day-night reversal, daytime napping and other causes of nighttime insomnia. Careful instruction in sleep hygiene should be undertaken. Medication should be used only when the patient is on a stable dose of methadone and sleep hygiene counseling has failed. Trazodone or other non-benzodiazepine hypnotics are the treatments of choice.

Sedation and Withdrawal Symptoms: Occasionally patients report sedation several hours after dosing, with withdrawal symptoms and insomnia at night. This can be difficult to sort out. The sedation may simply represent the onset of sleep following a night of insomnia due to withdrawal. The methadone dose might be too high, causing excessive sleep during the day and inadequate sleep at night. The patient may have day-night reversal, independent of the methadone dose.

Other conditions*:* Patients may be anticipating that an increase in their dose will manage symptoms that have little to do with withdrawal. Common examples include depression, anxiety, irritable bowel syndrome, and some forms of chronic pain. The physician should identify these symptoms, explain to the patient the limitations of MMT, and assist the patient in finding an appropriate management strategy.

Diagnostic Criteria for Opioid Withdrawal

A. Either of the following:
    1) cessation of (or reduction in) opioid use that has been heavy and prolonged (several weeks or longer)
    2) administration of an opioid antagonist after a period of opioid use

B. Three (or more) of the following: developing within minutes to several days after Criterion A:

   1) dysphoric mood
   2) nausea or vomiting
   3) muscle aches
   4) lacrimation or rhinorrhea
   5) pupillary dilation, piloerection or sweating
   6) diarrhea
   7) yawning
   8) fever
   9) insomnia

C. The symptoms in Criterion B cause clinically significant distress or impairment in social, occupational or other important areas of functioning.

D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.

Tolerance

Tolerance is said to occur when higher doses are required over time to achieve the same effect, and the same dose has less effect over time. Tolerance to the psychoactive effects of opioids develops within days, and is lost within days.

Appendix L: Take-Home Dose Agreement

Things you are expected to do when you are allowed to get take-home methadone

Methadone is a strong drug, and when people are allowed to take it home from a methadone clinic or pharmacy, they have to be very careful with it. People could get sick or die if you do not follow the rules for take-home methadone. Here are some things you should know:

- A single dose of methadone can kill someone who is not used to taking it
- A single dose of methadone can kill someone who is taking another drug
- Children often die if they take methadone when they are not supposed to

You have to sign your name on this page before your doctor can give you take-home methadone.

When you sign your name, it means that you know you are expected to do the things below.

If you do not understand these things, ask your doctor to explain them to you.

If you still do not understand these things, you should not sign your name.

1. You are expected to store your take-home doses in a locked box, in a location where it won't be stolen or accidentally taken by another person. You are expected to show this locked box to your doctor if you are asked to.

2. You are expected to swallow your dose of methadone only on the day(s) they are prescribed. You are expected to take a full dose once every 24 hours. You should not take it more often or less often.

3. You are expected to swallow the methadone dose in front of the pharmacist on the day that you pick up your take-home doses.

4. You are expected to return all your used methadone bottles to the pharmacist before you get your next take-home doses.

5. You should not give, lend, or sell your take-home doses to anyone else. You know that selling methadone is against the law and that it is dangerous for other people.

6. You know that take-home doses are a privilege and not a right. You know that your doctor can stop giving you take-home doses if he or she thinks that is the right thing to do.

7. If your health stays the same and you do what you are supposed to with your take-home doses, and you continue to have regular and clean urine samples, then your take home doses will be continued and you will be given more doses to take home once every four weeks.

8. The methadone clinic or pharmacy does not have to replace your take-home doses if they are lost, spilled, thrown up or stolen. Stolen take-home doses should be reported to the local police department.

9. You know that your doctor, the pharmacist or the methadone clinic staff may tell you at any time that you have to bring in all your full and empty take-home methadone bottles for them

to check. If you don't bring in your bottles when they tell you to, they can stop giving you take-home doses or make you leave the program. They might also call the police.

10. You are expected to let your methadone doctor's office or clinic know if your address or phone number changes.

Signatures

_____	_____	_____
Patient's Name	Patient's Signature	Date
_____	_____	_____
Witness Name	Witness Signature	Date

Appendix M: Protocols for MMT and Pregnancy

Protocol for Inpatient Initiation (Finnegan 1991, Kaltenbach et al. 1998)

Methadone initiation should begin at the first sign of withdrawal. Based on our experience, the expected length of stay is approximately 5-7 days.

On day 1:	Provide 10-20mg of methadone as an initial dose at onset of withdrawal symptoms, followed by supplemental 5mg every 4-6 hours if withdrawal symptoms are present.
On day 2:	Provide previous day's total dose as a single morning dose, followed by supplemental 5mg doses every 4-6 hours for withdrawal symptoms.
On subsequent days:	Continue as above until comfortable on one daily dose with no supplemental medications over a 24 hour period.

Most patients will be controlled on a daily dose of between 20-35mg of methadone after the first 2-3 days.

Subsequent dose increases will be needed as outpatients.

Protocol for Outpatient Initiation and Early Stabilization

If patient declines to be monitored on a daily basis for methadone dosing, follow the CPSNL protocol for outpatient initiation and early stabilization of non-pregnant individuals. Frequent office visits every 3 days are recommended until the patient is stabilized on a maintenance dose.

1. Administer 10-20mg initial dose for first 3 days
2. Further dose increases of 5-15mg can occur every 3-5 days based on persistent withdrawal symptoms.

Alternatively, if patient can be re-assessed repeatedly during the day, the following outpatient protocol developed by Hoegerman and Schnoll (1991) can be considered.

1. Patient is advised to arrive at the MMT physician's office or clinic for first appointment of the morning.
2. On day 1: Assess for withdrawal. If withdrawal is mild to moderate, administer a starting dose of 15mg of methadone and observe for several hours for intoxication. Patient returns in the afternoon and is re-assessed for withdrawal. An additional 5-10mg of methadone may be provided.
3. On day 2: Administer previous day's total dose as a single dose in the morning and consider increasing dose by 10mg if still experiencing withdrawal. Additional doses for later on the day may still be needed.

4. On subsequent days: Administer methadone as above until patient can be converted to a single dose of methadone.

5. Do not exceed 35mg by day 3.

Maintaining a pregnant woman on methadone can continue as with any other patient. The patient should be seen every 1-2 weeks to re-assess her methadone dose.

Appendix N: Resources

Health Canada Office of Controlled Substances

Tel: (613) 946-5139 **Toll-free:** 1-866-358-0453

Website: www.hc-sc.gc.ca/ahc-asc/branch-dirgen/hecs-dgsesc/dscsp-psasc/index-eng.php

Health Canada Methadone Exemption Application

Website: http://www.hc-sc.gc.ca/hc-ps/pubs/precurs/meth_on-eng.php

College of Physicians and Surgeons of Newfoundland and Labrador

Tel: (709) 726-8546

Website: www.cpsnl.ca

Newfoundland and Labrador Pharmacy Board

Tel: (709) Tel: 709-753-5877 Toll-Free: 1-877-453-5877

Website: http://www.nlpb.ca/

Methadone Drug Interactions Information

Websites www.atforum.com or www.drug-interactions.com

Centre for Addiction and Mental Health
Tel: (416) 535-8501**Website**: www.camh.net

Opioid Treatment Centre (Eastern Health)
Website: http://www.health.gov.nl.ca/health/addictions/services.html
Tel: (709)752-4478 (24 hours)

Central Health – Addictions Services
Website: http://www.centralhealth.nl.ca/mental-health-addictions-services/

Western Health – Addictions Services
Website: http://www.westernhealth.nl.ca/index.php/programs-and-services/services-a-z/addiction-services

Labrador – Grenfell Health – Addiction Services
Website: http://www.lghealth.ca/index.php?pageid=91

Appendix O: Behavioural Addictions

It is increasingly recognized that behavioural addictions are significantly comorbid with substance use disorders, as well as occurring independently of substance abuse. Substance dependence can be characterized by continued use of a substance despite negative consequences from the continued use of that substance. Along with loss of control, substance dependence also encompasses compulsive seeking of the substance and formation of a pathological relationship with the substance. Patients with behavioural addictions share these characteristics.

Examples of behavioural addictions include:

- Problem or pathological gambling
- Compulsive sexual behaviours such as use of pornography or sex workers
- Compulsive shopping or spending
- Compulsive theft or criminal behaviour
- Compulsive exercise
- Eating disorders
- Compulsive work habits

The hallmark of a behavioural addiction is the inability to resist the impulse to engage in the behaviour that is harmful to oneself or others. Given the high incidence of comorbid behavioural addictions and substance use disorders, screening of patients for behavioural addictions at the initial evaluation and on an intermittent basis is recommended. Evaluation for behavioural addictions can 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 behavioural addictions:

- Gambling: South Oaks Gambling Screen
- Problem Gambling Severity Index
- Gamblers Anonymous 20 Questions
- Sexual Addiction Screening Test

Appendix P: Urine Drug Test Interpretation

The interpretation of urine drug test (UDT) requires consideration of a number of factors, including opioid metabolites, detection times, substances that cross react causing false positive results, and cut-off values that may lead to false negative results.

Opioids that metabolize to other prescribed opioids:

Some opioids metabolize into other prescribed opioids. These metabolites can be detected in UDT and, if not recognized as metabolites, may be misinterpreted as unsanctioned opioid use.

Codeine	Morphine, hydrocodone
Morphine	Hydromorphone
Hydrocodone	Hydromorphone
Heroin	Morphine, (codeine contaminant)

Buprenorphine, fentanyl, hydromorphone, meperidine, methadone and oxycodone do not metabolize to other prescribed opioids.

Detection times:

Detection times are dependent on the rate of clearance of the substances measured. The times listed in the table below are approximate, and will depend on the specific testing materials used. With point-of-care testing, the detection times will be provided by the vendor. With hospital testing, it is recommended that the detection times be ascertained from the laboratory. It is important to recognize that some substances (barbiturates, benzodiazepines and cannabinoids) can be detected for weeks after last use.

Amphetamines	2 days
Barbiturates	Short acting 1 day
	Long acting 2 to 3 weeks
Benzodiazepines	Therapeutic dose 3 or more days (depends on half-life of specific drug)
	Extended use: 4 to 6 weeks
Cocaine	2 to 4 days
Opioids	2 to 3 days
Cannabinoids	Light smoker (1 joint) 2 to 3 days
	Moderate smoker (four joints a week) five days. Daily smoker 10 days. Chronic smoker four weeks

False positive tests

Many drugs can cross-react with immunoassay tests causing false positive results. When an unexpected UDT result occurs, it is important to exclude the possibility of a false positive test. The following lists some substances that can cause false positive tests.

- **THC**: ketoprofen, naproxen, ibuprofen, sustiva, pantoprazole, promethazine, riboflavin, marinol, sativex, hemp seed oil
- **Opioid**: poppy seeds, chlorpromazine, rifampin, dextromethorphan, quinine, fluoroquinolones
- **Methadone**: quetiapine, methotrimeprazine
- **Benzodiazepines**: sertraline, oxaprozin, flurbiprofen, indomethacin, ketoprofen
- **Amphetamine**: Vicks vapor nasal inhaler, ephedrine, pseudoephedrine, tramline, ciprofloxacin, mefanamic acid, labetalol, methylphenidate, trazodone, desipramine, bupropion, propranolol, phenylephrine, mexilitine, selegiline, amantadine, ranitidine, metronidazole, phenothiazines, some diet pills
- **Cocaine**: salicylates, fluconazole

Cut-off values

Immunoassay tests have artificially established cut-off values in an attempt to reduce the incidence of false positive tests. This is largely established for workforce testing to minimize false positive tests and resulting consequences. As a result, a substance may be present, but not reported as positive if it exists at levels below the artificial cut-off value. This leads to possible false negative results. The higher the cut-off value, the higher the risk of false negative results. It is recommended that physicians consult with the laboratory to determine the specific cut-off values for the tests used.

Appendix Q: Sample Tapering Readiness Questionnaire

When a client indicates that he or she would like to leave treatment, a number of questions should be asked to determine if the person is ready to taper from methadone. Consider the following questions:

1. Have you been abstaining from illegal drugs, such as cocaine and non-prescribed opioids and benzodiazepines?

   Yes No

2. Do you think you are able to cope with difficult situations without using drugs?

   Yes No

3. Are you employed or in school?

   Yes No

4. Are you staying away from people who use drugs and illegal activities?

   Yes No

5. Have you gotten rid of your “works”/“outfit”?

   Yes No

6. Are you living in a neighbourhood that doesn’t have a lot of drug use, and are you comfortable there?

   Yes No

7. Are you living in a stable family relationship?

   Yes No

8. Do you have non-drug-using friends that you spend time with?

   Yes No

9. Do you have friends or family who would be helpful during a taper?

   Yes No

10. Have you been participating in counseling that has been helpful?

    Yes No

11. Does your counselor think you are ready to taper?

    Yes No

12. Do you think you would ask for help when you were feeling bad during a taper?

    Yes No

13. Have you been on methadone for a long time (> 1 year)?

    Yes No

14. Are you in good mental and physical health?

    Yes No

15. Do you want to get off methadone?

    Yes No

The more questions the client can honestly answer by checking “yes,” the greater the likelihood that he or she is ready to taper from methadone. Consider that each “no” response represents an area that probably needs work to increase the odds of a successful taper.

Appendix R: Emergency Department Management of Methadone Overdose

*** NOTE: The methadone prescriber may send this form to the ED to assist in managing a patient with a suspected methadone overdose.**

Copyright © Centre for Addiction and Mental Health (CAMH), Methadone Maintenance Treatment: A Physician's Guide (Toronto: CAMH, 2007). This appendix may be reproduced freely for use by physicians and treatment staff, but must be reproduced in its entirety.

Patient:_____

Doctor:_____

Poison Centre Phone #:_____ Doctor Phone #:

_____

Relevant details (to be completed by methadone provider):

- Usual methadone dose
- Dose of the suspected overdose (if known):
- Concurrent alcohol, benzodiazepine or other drug use
- Medications
- Relevant medical/psychiatric history
- Circumstances of the overdose (intentional or accidental):

Clinical features of methadone overdose:

Methadone acts for at least 24 hours, much longer than other opioids. Symptoms begin up to 10 hours after the overdose. Early symptoms include nodding off, drowsiness, slurred speech and emotional lability. Respiratory depression occurs later.

Emergency care protocol for managing suspected methadone overdose

Monitoring:

- Check frequently for vital signs, respiratory rate and O2 sat
- Hold a brief conversation to assess alertness
- ECG and cardiac monitoring to check for prolonged QTc interval and ventricular arrhythmias (methadone can cause torsades de pointes)

Medical management with intubation or naloxone

Naloxone is a safe treatment in patients who are not physically dependent on opioids (e.g., patients not in methadone therapy who took methadone at a party). For methadone or opioid-dependent patients, intubation avoids risks of naloxone-induced withdrawal. Intubation is necessary if:

- RR < 12; hypercapnia; persistent desaturation despite supplemental oxygen
- Patient fails to respond to naloxone within 2 min

Naloxone precautions

- Ventricular dysrhythmias and cardiac arrest can occur with naloxone-induced withdrawal, especially if patients are withdrawing from other substances.
- Patients in naloxone-induced withdrawal may become agitated and leave against medical advice.
- Naloxone can induce emesis.

Above risks are avoided with intubation.

Naloxone dosing

- If the patient has severe respiratory depression, give 2.0 mg naloxone IV.
- If there is minimal respiratory depression, give 0.01 mg/kg weight to avoid precipitating withdrawal.
- If there is no response after the initial dose, repeat naloxone two to four mg every two to three minutes.
- If there is no response after 10-20 mg naloxone, search for other causes for the coma.
- If the patient responds to naloxone, infuse at 2/3 of the effective dose per hour.
- Give a bolus of 1/2 the effective dose 15 to 20 minutes after starting infusion.
- Titrate dose to avoid withdrawal, while maintaining adequate non-assisted respirations.

Recommended emergency care observation periods

- Observe for at least 10 hours post-overdose.
- Discharge if patient has been completely asymptomatic after ten hours observation.
- If patient becomes symptomatic at any time during the 10 hours, monitor for at least 24 hours post-overdose.
- If patient is intubated or on naloxone, continue intubation/naloxone for at least 24 hours post-overdose.
- Monitor for at least sex hours after naloxone or intubation is discontinue

Discharge instructions: Tell patient not to take any methadone, alcohol or sedating drugs until seen by methadone physician the next day. Have a family member or support person observe overnight, and call an ambulance if the patient appears more drowsy, is difficult to arouse or snores much more loudly than usual.

Appendix S: List of Acronyms

AA - Alcoholics Anonymous

AMA - Against Medical Advice

BP - Blood Pressure

CA - Cocaine Anonymous

CAGE - Cut-Down, Annoyed, Guilty, Eye-Opener Test

CAMH - Centre for Addiction and Mental Health

CBT - Cognitive Behavioural Therapy

CFPC - College of Family Physicians of Canada

CHC - Community Health Centre

CNCP - Chronic Non-Cancer Pain

CNS - Central Nervous System

COPD - Chronic Obstructive Pulmonary Disease

CPSBC - College of Physicians and Surgeons of British Columbia

CPSNL – College of Physicians and Surgeons of Newfoundland and Labrador

CPSNS - College of Physicians and Surgeons of Nova Scotia

CPSO - College of Physicians and Surgeons of Ontario

CSC - Correctional Services of Canada

DMF - Delegated Medical Function

DSM IV - Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition

ECG - Electrocardiogram

ED - Emergency Department

EDDP - 2-Ethylidene-1, 5 Dimethyl-3, 3-Diphenylpyrrolidine

EIA - Enzyme Immunoassay

EMIT - Enzyme Multiplied Immunoassay Technique

GHN - Growth Hormone Normal

HCV - Hepatitis C Virus

HIV/HCD - Human Immunodeficiency Virus

IPC - Inter-Professional Collaboration

LMP - Last Menstrual Period

MI - Motivational Interviewing

MDU – Medical Detox Units

MMT - Methadone Maintenance Treatment

NA - Narcotics Anonymous

NAS - Neonatal Absence Syndrome

NIHBI - Non-Insured Health Benefits (NS Pharmacare)

NPO - Nothing by Mouth

OAT - Opioid Agonist Therapy

ODT - Opioid Dependence Treatment

PTSD - Post Traumatic Stress Disorder

Appendix T: Checklist

CPSNL Methadone Maintenance Treatment (MMT) Standards and Guidelines

Name of Patient: _____
D.O.B. of Patient and/or MCP No.: _____
Date of MMT Initiation: _____

	Yes	No
Initial Patient Assessment Form (Appendix C) completed? *Applicable only for new MMT patients after May 1, 2013; if not applicable to this patient, circle* **"Not Applicable"**	❑	❑
Methadone Maintenance Treatment Agreement (Appendix D) signed by patient? *Applicable to all MMT patients*	❑	❑
Patient initiation/Continuation to MMT Form (Appendix E) filed with the College? *Applicable to all MMT patients*	❑	❑
Physician-Pharmacist Treatment Agreement Letter (Appendix G) signed? *Applicable to all MMT patients*	❑	❑
Take-Home Dose Agreement (Appendix L) signed? *Applicable to all MMT patients with take-home privileges; if no applicable to this patient, circle* **"Not Applicable"**	❑	❑
If the patient has a history of cardiac disease or is prescribed a dose above 150 mg od, has ECG been obtained? *If not applicable to this patient, circle* **"Not Applicable"**	❑	❑

* NOTE: You may be required to submit to the College a copy of the completed checklist as part of a quality assurance audit.

Glossary

Abuse, drug

Any use of an illegal drug, or the intentional self-administration of a medication for a non-medical purpose such as altering one's state of consciousness, e.g., "getting high." (Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010)

Addiction

A primary, chronic, neurobiological disease with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviours that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving. (Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010)

Agonist

Drugs that interact with receptor sites to cause the same effect that natural chemicals would case at these sites. Karch, A, M. (2008). *Focus on nursing in pharmacology.* (4th ed.). Philadelphia: Wolters Kluwer/Lippincott Williams and Wilkins.

Agonist (Adopted 99.10.14)
A substance that acts at a neuronal receptor to produce effects similar to those of a reference psychoactive substance, e.g. methadone is an agonist at the opioid receptors.

Antagonist

Drugs that combine with receptors that do not begin a change in cell function. When antagonists bind to receptors, agonists are prevented from binding and causing an action. Gutierrez, K. (2008). *Pharmacotherapeutics: Clinical reasoning in primary care* (2nd ed.). Saunders: St. Louis.

Antagonist (Adopted Canadian Society of Addiction Medicine October 14, 1999)

A substance that counteracts the effects of a reference psychoactive substance by inhibiting or reversing its effects at a neuronal receptor site, e.g. naltrexone acts as an antagonist at the opioid receptor.

Concurrent Disorders (Adopted Canadian Society of Addiction Medicine October 14, 1999)
The presence of one or more primary, physical and/or psychiatric disorders that have an interactive effect on the course of Substance Dependence and require specific diagnosis and treatment in order to achieve stabilization and/or recovery.

Controlled Substance

There are many controlled substances listed under the *Controlled Substance Act.* These drugs are grouped under schedules. Below are examples of some of the better known drugs within each Schedule:

- Schedule I contains drugs made from the opium poppy such as heroin, codeine; drugs made from coca such as cocaine; and synthetically derived drugs such as methadone.

- Schedule II contains cannabis (marijuana) and its derivatives.
- Schedule III contains drugs such as amphetamines and lysergic acid diethylamide (LDS).
- Schedule IV contains drugs such as benzodiazepines and barbiturates.
- Schedule V and VI contain precursors required to produce controlled substances (National Association of Pharmacy Regulatory Authorities, 2002-2004).

Craving (Adopted Canadian Society of Addiction Medicine October 14, 1999)

A bio-psychological arousal and urge to return to addictive behaviour, characterized by a strong desire, pre-occupation and possible impulsivity.

Contingency Management

A type of treatment used in the mental health and substance abuse fields. Patients are rewarded (or less often, punished) for their behaviour; generally, adherence to or failure to adhere to program rules and regulations or their treatment plan.

Dependence, Physical

A state of adaptation manifested by a drug class-specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist. (Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010)

Diversion

The intentional transfer of a controlled substance from legitimate distribution and dispensing channels. (Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010)

Dose, stable

A “pharmacologically stable dose” is one that produces a fairly steady plasma level; it is established when the total daily dose is fixed for at least two weeks and:

1) frequency is scheduled and spread throughout the day, AND/OR

2) at least 70% of the prescribed opioid is controlled release.

Double-doctoring

Receiving a prescription for a narcotic, and then seeking and receiving another prescription or narcotic from a different practitioner without disclosing to that practitioner particulars of every prescription or narcotic obtained within the previous 30 days.(Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010)

Half-life

The time required for half of the total drug amount to be eliminated from the body. Generally after five half-lives, 97% of a drug will be eliminated.

Pharmacotherapeutics for Advanced Practice – A Practical Approach, Virginia Poole Arcangelo and Andrew M. Petersen, Second Edition, 2006.

Harm Reduction

A continuum of services that represent a philosophical, pragmatic approach to providing care while minimizing the negative outcomes associated with substance use. The focus is goal oriented, humanistic and in keeping with a cost benefit awareness. (Pauly, Goldstone, McCall, Gold and Pyne, 2007). Pauly, B., Goldstone, I., McCall, J., Gold, F., & Payne, S. (2007). The ethical, legal and social context of harm reductions. *Canadian Nurse, 103,* 19–23.

Maintenance Therapy (Adopted 01.10.19)

Treatment of Substance Dependence by a prescription drug, to prevent withdrawal and reduce the harm associated with a particular method of administration, attendant dangers to health and/or social consequences, e.g. methadone for Opioid Dependence or nicotine replacement therapy (NRT) for tobacco.

Misuse, opioid

Use of an opioid in ways other than those intended by the prescribing physician (sometimes also called problematic opioid use). (Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010)

Narcotic

Any drug included in the "Schedule" under the Controlled Drugs and Substances Act: Narcotic Control Regulations.
(http://laws-lois.justice.gc.ca/eng/regulations/C.R.C., c. 1041/index.html)

Opiate

A naturally-occurring or semi-synthetic compound derived from the opium poppy (papaver somnifer) (College of Physicians and Surgeons of Alberta, 2005).

Opioid

A compound having actions or properties similar to opiates. A broader term encompassing all opiates (such as heroin, morphine and codeine), as well as synthetic opiate-like compounds (such as methadone and fentenyl) (College of Physicians and Surgeons of Alberta, 2005).
A family of drugs that act by attaching to endogenous mu, kappa and delta receptors in the brain and share a common set of clinical effects, including analgesia, sedation, constipation, and respiratory depression. **Note**: Reference throughout this document to specific pharmaceutical products as examples does not imply endorsement of any of these products.

Pharmacodynamics

The set of processes by which drugs produce specific biochemical or physiological changes in the body-how the drug acts on the body

Pharmacotherapeutics for Advanced Practice – A Practical Approach, Virginia Poole Arcangelo and Andrew M. Petersen, Second Edition, 2006 (Archangelo and Peterson, 2006).

Pharmacokinetics

Examining the absorption, distribution, metabolism and excretion of a drug, the onset of action, the half life, peak effect and duration of effects – how the body acts on the drug.

Karch, A, M. (2008). *Focus on nursing in pharmacology.* (4th ed.). Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins.

Split doses

An alternative way of providing methadone to clients, consisting of two or more doses per day (so it is not ingested all at one time). It is used for clients who have demonstrated "rapid metabolism" of their once daily methadone dose (e.g. during third trimester of pregnancy) or are on medications that have been shown to induce rapid metabolism of methadone (i.e. certain HIV medications). A consultation with a experienced MMT provider should be considered in these circumstances. Split doses do not necessarily have to be equal; twice-daily observed ingestion may be necessary

(College of Physicians and Surgeons of Alberta, 2005).

Stable daily dose

Optimal daily dose of methadone that will relieve withdrawal symptoms, block opioid-induced euphoria and reduce drug cravings without sedation or other significant side effects

(College of Physicians and Surgeons Ontario, 2005).

Steady state

A constant mean concentration of a drug in the body, there are peaks and troughs in the drug level, but the fluctuations remain within a constant range

Pharmacotherapeutics for Advanced Practice – A Practical Approach, Virginia Poole Arcangelo and Andrew M. Petersen, Second Edition, 2006. (Archangelo and Peterson, 2006).

Substance

Any drug with pleasant psychoactive effects and addiction potential, including alcohol, illegal drugs, and prescription drugs.

(Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010)

Substance abuse (American Psychiatric Association, 1994)

A. A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by one (or more) of the following, occurring within a 12 month period:
    1. recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home (e.g. repeated absences or poor work performance related to substance use; substance-related absences, suspensions, or expulsions from school; neglect of children or household).
    2. recurrent substance use in situations in which it is physically hazardous (e.g. driving an automobile or operating a machine when impaired by substance use).
    3. recurrent substance-related legal problems (e.g. arrests for substance-related disorderly conduct)
    4. continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance (e.g. arguments with spouse about consequences of intoxication, physical fights)
B. The symptoms have never met the criteria of Substance Dependence for this class of substance.

Substance dependence

See addiction.

Substance dependence

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 (American Psychiatric Association, 1994)

A. Tolerance, as defined by either of the following:
    1. a need for markedly increased amounts of the substance to achieve intoxication or desired effect; or
    2. markedly diminished effect with continued use of the same amount of the substance.
B. Withdrawal, as manifested by either of the following:
    1. the characteristic withdrawal syndrome for the substance; or
    2. the same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms.
C. The substance is often taken in larger amounts or over a longer period than was intended.
D. There is a persistent desire or unsuccessful efforts to cut down or control substance use.
E. 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.
F. Important social, occupational, or recreational activities are given up or reduced because of substance use.
G. 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).

With physiological dependence: evidence of tolerance or withdrawal (i.e. either Item 1 or 2 is present).
Without physiological dependence: no evidence of tolerance or withdrawal (i.e. neither Item 1 nor 2 is present).

Substance misuse

The use of a psychoactive substance (drug or alcohol) for a purpose other than that for which it was intended, and that cause's physical, social, and psychological harm. The term is also used to represent the pattern of use: experimental, recreational and dependent (Rassol, 2002).

Rassol, G. (2002) Substance misuse and mental health: An Overview. Nursing Standard, 16, 46-52.

Substance tolerance

A neurological adaptation to the psychoactive effects of a substance; more of the drug is required to achieve the same effect. Tolerance develops quickly to the psychoactive effects of alcohol and opioids. Highly tolerant clients can behave almost normally after consuming opioid doses that would be fatal in non-tolerant clients (Kahan and Wilson, 2002). Tolerance to the psychoactive effects of opioids develops within days, and is lost within days (CPSO, 2005).
A state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more opioid effects over time.

(Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010)

Substance Use Disorders (Adopted Canadian Society of Addiction Medicine October 17, 2003)
A category of two disorders, namely, Substance Abuse and Substance Dependence, as in DSM IV.

Substance withdrawal

Characteristic syndrome produced by abrupt cessation of a drug.

(Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010)

Tapering

A gradual decrease in a dose of a drug; could result in a lower daily dose or cessation of the drug.

(Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010)

Titration

A technique of adjusting a dose until a stable/optimal dose is reached; usually means gradually increasing the dose to allow the body to develop tolerance and minimize adverse effects.

(Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010)

Tolerance

A state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more opioid effects over time.

Withdrawal

Characteristic syndrome produced by abrupt cessation of a drug.

(Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain 2010)

Bibliography

Abramson DW, Quinn DK, Stern TA (2008) Methadone-Associated QTc Prolongation: A Case Report and Review of the Literature. Prim Care Companion J Clin Psychiatry 10: 470-6

Albion C, Shkrum M, Cairns J (2010) Contributing factors to methadone-related deaths in ontario. Am J Forensic Med Pathol 31: 313-9

Amass L, Bickel WK, Crean JP, Higgins ST, Badger GJ (1996) Preferences for clinic privileges, retail items and social activities in an outpatient buprenorphine treatment program. J Subst Abuse Treat 13: 43-9

Amass L, Kamien JB, Mikulich SK (2001) Thrice-weekly supervised dosing with the combination buprenorphine-naloxone tablet is preferred to daily supervised dosing by opioid-dependent humans. Drug Alcohol Depend 61: 173-81

Amato L, Davoli M, Minozzi S, Ali R, Ferri M (2005) Methadone at tapered doses for the management of opioid withdrawal. Cochrane Database Syst Rev: CD003409

Anchersen K, Clausen T, Gossop M, Hansteen V, Waal H (2009) Prevalence and clinical relevance of corrected QT interval prolongation during methadone and buprenorphine treatment: a mortality assessment study. Addiction 104: 993-9

Archie C (1998) Methadone in the management of narcotic addiction in pregnancy. Curr Opin Obstet Gynecol 10: 435-40

Astals M, Domingo-Salvany A, Buenaventura CC, Tato J, Vazquez JM, Martin-Santos R, Torrens M (2008) Impact of substance dependence and dual diagnosis on the quality of life of heroin users seeking treatment. Subst Use Misuse 43: 612-32

Aszalos R, McDuff DR, Weintraub E, Montoya I, Schwartz R (1999) Engaging hospitalized heroin-dependent patients into substance abuse treatment. J Subst Abuse Treat 17: 149-58

Australian Department of Health and Aging (2003) Principles of Drug Addiction Treatment: A Research-Based Guide, Canaberra, Australia

Backmund M, Schutz CG, Meyer K, Eichenlaub D, Soyka M (2003) Alcohol consumption in heroin users, methadone-substituted and codeine-substituted patients--frequency and correlates of use. Eur Addict Res 9: 45-50

Ball JC, Lange WR, Myers CP, Friedman SR (1988) Reducing the risk of AIDS through methadone maintenance treatment. J Health Soc Behav 29: 214-26

Banta-Green CJ, Maynard C, Koepsell TD, Wells EA, Donovan DM (2009) Retention in methadone maintenance drug treatment for prescription-type opioid primary users compared to heroin users. Addiction 104: 775-83

Bao YP, Liu ZM, Epstein DH, Du C, Shi J, Lu L (2009) A meta-analysis of retention in methadone maintenance by dose and dosing strategy. Am J Drug Alcohol Abuse 35: 28-33

Baron MJ, McDonald PW. Significant pain reduction in chronic pain patients after detoxification from high-dose opioids. Journal of Opioid Management (2006) Sep;2(5):277-82.

Beauverie P, Furlan V, Edel YA (2001) Slow metabolism and long half life of methadone in a patient with lung cancer and cirrhosis. Ann Med Interne (Paris) 152 Suppl 7: 50-2

Bell GL, Lau K (1995) Perinatal and neonatal issues of substance abuse. Pediatr Clin North Am 42: 261-81

Berghella V, Lim PJ, Hill MK, Cherpes J, Chennat J, Kaltenbach K (2003) Maternal methadone dose and neonatal withdrawal. Am J Obstet Gynecol 189: 312-7

Binder T, Vavrinkova B (2008) Prospective randomised comparative study of the effect of buprenorphine, methadone and heroin on the course of pregnancy, birthweight of newborns, early postpartum adaptation and course of the neonatal abstinence syndrome (NAS) in women followed up in the outpatient department. Neuro Endocrinol Lett 29: 80-6

Bleich A, Gelkopf M, Schmidt V, Hayward R, Bodner G, Adelson M (1999) Correlates of benzodiazepine abuse in methadone maintenance treatment. A 1 year prospective study in an Israeli clinic. Addiction 94: 1533-40

Blinick G, Wallach RC, Jerez E (1969) Pregnancy in narcotics addicts treated by medical withdrawal. The methadone detoxification program. Am J Obstet Gynecol 105: 997-1003

Brands B, Blake J, Marsh DC, Sproule B, Jeyapalan R, Li S (2008) The impact of benzodiazepine use on methadone maintenance treatment outcomes. J Addict Dis 27: 37-48

Brands B, Blake J, Sproule B, Gourlay D, Busto U (2004) Prescription opioid abuse in patients presenting for methadone maintenance treatment. Drug Alcohol Depend 73: 199-207

Brands J, Brands B, Marsh D (2000) The expansion of methadone prescribing in Ontario, 1996-1998. Addiction Research 8: 485-496

Breslin KT, Malone S (2006) Maintaining the viability and safety of the methadone maintenance treatment program. J Psychoactive Drugs 38: 157-60

Bruera E, Palmer JL, Bosnjak S, Rico MA, Moyano J, Sweeney C, Strasser F, Willey J, Bertolino M, Mathias C, Spruyt O, Fisch MJ (2004) Methadone versus morphine as a first-line strong opioid for cancer pain: a randomized, double-blind study. J Clin Oncol 22: 185-92

Burke BL, Arkowitz H, and Dunn C (2002) The eficacy of motivational interviewing and its adaptations: What we know so far. In W.R. Miller and S. Rollnick (Eds.), Motivational Intervewing: Preparing People for Change pp 217-250. New York: Guilford Press.

Byrne A (2009) Concerns about consensus guidelines for QTc interval screening in methadone treatment. Ann Intern Med 151: 216; author reply 218-9

Cacciola JS, Alterman AI, Rutherford MJ, McKay JR, Mulvaney FD (2001) The relationship of psychiatric comorbidity to treatment outcomes in methadone maintained patients. Drug Alcohol Depend 61: 271-80

Callaly T, Trauer T, Munro L, Whelan G (2001) Prevalence of psychiatric disorder in a methadone maintenance population. Aust N Z J Psychiatry 35: 601-5

CAMH (2004) Centre for Addiction and Mental Health. Issac P, Kalvik A, Brands J, Janecek E (Eds). Methadone Maintenance: A Pharmacist's Guide to Treatment, 2nd edition.

CAMH (November 24, 2010) Centre for Addiction and Mental Health, Personal communication letter by CAMH pharmacists Eva Janecek, Annie Kalvik, Pearl Isaac, Beth Sproule.

Caplehorn JR, Bell J (1991) Methadone dosage and retention of patients in maintenance treatment. Med J Aust 154: 195-9

Caplehorn JR, Dalton MS, Cluff MC, Petrenas AM (1994) Retention in methadone maintenance and heroin addicts' risk of death. Addiction 89: 203-9

Caplehorn JR, Drummer OH (1999) Mortality associated with New South Wales methadone programs in 1994: lives lost and saved. Med J Aust 170: 104-9

Caplehorn JR, Drummer OH (2002) Fatal methadone toxicity: signs and circumstances, and the role of benzodiazepines. Aust N Z J Public Health 26: 358-62; discussion 362-3

Caplehorn JR, Ross MW (1995) Methadone maintenance and the likelihood of risky needle-sharing. Int J Addict 30: 685-98

Caputo F, Addolorato G, Domenicali M, Mosti A, Viaggi M, Trevisani F, Gasbarrini G, Bernardi M, Stefanini GF (2002) Short-term methadone administration reduces alcohol consumption in non-alcoholic heroin addicts. Alcohol Alcohol 37: 164-8

Carpenter KM, Brooks AC, Vosburg SK, Nunes EV (2004) The effect of sertraline and environmental context on treating depression and illicit substance use among methadone maintained opiate dependent patients: a controlled clinical trial. Drug Alcohol Depend 74: 123-34

Chakrabarti A, Woody GE, Griffin ML, Subramaniam G, Weiss RD (2010) Predictors of buprenorphine-naloxone dosing in a 12-week treatment trial for opioid-dependent youth: secondary analyses from a NIDA Clinical Trials Network study. Drug Alcohol Depend 107: 253-6

Chang G, Carroll KM, Behr HM, Kosten TR (1992) Improving treatment outcome in pregnant opiate-dependent women. J Subst Abuse Treat 9: 327-30

Chasnoff IJ, Hatcher R, Burns WJ (1982) Polydrug- and methadone-addicted newborns: a continuum of impairment? Pediatrics 70: 210-3

Cheung O, Sterling RK, Salvatori J, Williams K, Hubbard S, Luketic VA, Stravitz TR, Sanyal AJ, Contos MJ, Mills S, Shiffman ML (2010) Mild Alcohol Consumption is Not Associated With Increased Fibrosis in Patients With Chronic Hepatitis C. J Clin Gastroenterol 45: 76-82

Chutuape MA, Silverman K, Stitzer M (1999a) Contingent reinforcement sustains post-detoxification abstinence from multiple drugs: a preliminary study with methadone patients. Drug Alcohol Depend 54: 69-81

Chutuape MA, Silverman K, Stitzer ML (1999b) Use of methadone take-home contingencies with persistent opiate and cocaine abusers. J Subst Abuse Treat 16: 23-30

Chutuape MA, Silverman K, Stitzer ML (2001) Effects of urine testing frequency on outcome in a methadone take-home contingency program. Drug Alcohol Depend 62: 69-76

Collège des médecins du Québec and Ordre des pharmaciens du Québec (2000) Clinical guidelines and procedures for the use of methadone in the maintenance treatment of opioid dependence, Quebec City

Corkery JM, Schifano F, Ghodse AH, Oyefeso A (2004) The effects of methadone and its role in fatalities. Hum Psychopharmacol 19: 565-76

Cornish R, Macleod J, Strang J, Vickerman P, Hickman M (2010) Risk of death during and after opiate substitution treatment in primary care: prospective observational study in UK General Practice Research Database. BMJ 341: c5475

CPSO (2009) College of Physicians and Surgeons of Ontario Annual Report 2009, Toronto, ON

Crisostomo RA, Schmidt JE, Hooten WM, Kerkvliet JL, Towsend CO, Bruce BK. (2008) Withdrawal of analgesic medication for chronic low-back pain patients: improvement in outcomes of multidisciplinary rehabilitation regardless of surgical history. Am J Phys Med Rehabil;87(7): 527-36.

Currie J (2001) Best Practices Treatment and Rehabilitation for Women with Substance Use Problems. Health Canada, Ottawa

Cushman P, Jr. (1978) Methadone maintenance: long-term follow-up of detoxified patients. Ann N Y Acad Sci 311: 165-72

Cushman P, Jr. (1981) Detoxification after methadone maintenance treatment. Ann N Y Acad Sci 362: 217-30

Darke S, Ross J, Mills K, Teeson M, Williamson A, and Harvard A. Benzodiazepine use among heroin users: baseline use, current use and clinical outcome. Drug Alcohol Rv 2010; 29(3): 250-5.

Darke S, Duflou J, Torok M. The comparative toxicology and major organ pathology of fatal methadone and heroin toxicity cases. Drug Alcohol Depnd. 2010:106(1):1-6.

Darke S, Duflou J, Tork M. Drugs and voilent death: comparative toxicology of moicide and non-substance toxicity suicide victoms. Addiction 2009 Jun; 104(6): 1000-1005.
Dashe JS, Jackson GL, Olscher DA, Zane EH, Wendel GD, Jr. (1998) Opioid detoxification in pregnancy. Obstet Gynecol 92: 854-8
Dashe JS, Sheffield JS, Olscher DA, Todd SJ, Jackson GL, Wendel GD (2002) Relationship between maternal methadone dosage and neonatal withdrawal. Obstet Gynecol 100: 1244-9
Dean AJ, Bell J, Mascord DJ, Parker G, Christie MJ (2002) A randomised, controlled trial of fluoxetine in methadone maintenance patients with depressive symptoms. J Affect Disord 72: 85-90
Degenhardt L, Randall D, Hall W, Law M, Butler T, Burns L (2009) Mortality among clients of a state-wide opioid pharmacotherapy program over 20 years: risk factors and lives saved. Drug Alcohol Depend 105: 9-15
DeMaria PA, Sterling R, Weinstein SP. The effect of stimulant and sedative use on treatment outcome of patients admitted to methadone maintenance treatment. Am J Addict. 2000 Spring; 9(2): 145-53.
Department of Health (England) (2007) Drug Misuse and Dependence: UK Guidelines on Clinical Managment. In: Department of Health (England) (ed), London
Dhalla IA, Mamdani MM, Sivilotti ML, Kopp A, Qureshi O, Juurlink DN (2009) Prescribing of opioid analgesics and related mortality before and after the introduction of long-acting oxycodone. CMAJ 181: 891-6
Doberczak TM, Kandall SR, Friedmann P (1993) Relationship between maternal methadone dosage, maternal-neonatal methadone levels, and neonatal withdrawal. Obstet Gynecol 81: 936-40
Dole VP, Nyswander M (1965) A Medical Treatment for Diacetylmorphine (Heroin) Addiction. A Clinical Trial with Methadone Hydrochloride. JAMA 193: 646-50
Dole VP, Nyswander ME (1966) Rehabilitation of heroin addicts after blockade with methadone. N Y State J Med 66: 2011-7
Doverty M, Somogyi AA, White JM, Bochner F, Beare CH, Menelaou A, Ling W (2001) Methadone maintenance patients are cross-tolerant to the antinociceptive effects of morphine. Pain 93: 155-63
Drozdick J, 3rd, Berghella V, Hill M, Kaltenbach K (2002) Methadone trough levels in pregnancy. Am J Obstet Gynecol 187: 1184-8
Drucker E, Rice S, Ganse G, Kegley J, Bonuck K, Tuchman E (2007) The Lancaster Office Based Opiate Treatment Program: A Case Study and Prototype for Community Physicians and Pharmacists Providing Methadone Maintenance Treatment in the United States. Addictive Disorders & Their Treatment 6: 121-135
Eap CB, Buclin T, Baumann P (2002) Interindividual variability of the clinical pharmacokinetics of methadone. Implications for the treamtnet of opioid dependence. Clinical Pharamcokinetics 41(14): 1153-1193.
Ehret GB, Voide C, Gex-Fabry M, Chabert J, Shah D, Broers B, Piguet V, Musset T, Gaspoz JM, Perrier A, Dayer P, Desmeules JA (2006) Drug-induced long QT syndrome in injection drug users receiving methadone: high frequency in hospitalized patients and risk factors. Arch Intern Med 166: 1280-7
Elkader AK, Brands B, Dunn E, Selby P, Sproule BA (2009) Major depressive disorder and patient satisfaction in relation to methadone pharmacokinetics and pharmacodynamics in stabilized methadone maintenance patients. J Clin Psychopharmacol 29: 77-81
Ellwood DA, Sutherland P, Kent C, O'Connor M (1987) Maternal narcotic addiction: pregnancy outcome in patients managed by a specialized drug-dependency antenatal clinic. Aust N Z J Obstet Gynaecol 27: 92-8

Ernst E, Bartu A, Popescu A, Ileutt KF, Hansson R, Plumley N (2002) Methadone-related deaths in Western Australia 1993-99. Aust N Z J Public Health 26: 364-70
Faggiano F, Vigna-Taglianti F, Versino E, Lemma P (2003) Methadone maintenance at different dosages for opioid dependence. Cochrane Database Syst Rev: CD002208
Fairbank JA, Dunteman GH, Condelli WS (1993) Do methadone patients substitute other drugs for heroin? Predicting substance use at 1-year follow-up. Am J Drug Alcohol Abuse 19: 465-74
Fanoe S, Hvidt C, Ege P, Jensen GB (2007) Syncope and QT prolongation among patients treated with methadone for heroin dependence in the city of Copenhagen. Heart 93: 1051-5
Fareed A, Vayalapalli S, Byrd-Sellers J, Casarella J, Drexler K, Amar R, Smith-Cox J, Lutchman TS (2010) Onsite QTc interval screening for patients in methadone maintenance treatment. J Addict Dis 29: 15-22
Farrell M, Neeleman J, Gossop M, Griffiths P, Buning E, Finch E, Strang J (1996) A Review of the Legislation, Regulation and Delivery of Methadone in 12 Member States of the European Union. The European Commission, Brussels, Belgium
Fiellin DA, O'Connor PG, Chawarski M, Pakes JP, Pantalon MV, Schottenfeld RS (2001) Methadone maintenance in primary care: a randomized controlled trial. JAMA 286: 1724-31
Finnegan LP (1978) Management of pregnant drug-dependent women. Ann N Y Acad Sci 311: 135-46
Finnegan LP (1991) Treatment issues for opioid-dependent women during the perinatal period. J Psychoactive Drugs 23: 191-201
Finnegan LP, Kaltenbach K (1992) Neonatal abstienence syndrome. In: Hoekelman, Nelson (eds) Primary Pediatric Care. Mosby Yearbook Inc., St. Louis
Finnegan LP, Kron RE, Connaughton JF, Emich JP (1975) Assessment and treatment of abstinence in the infant of the drug-dependent mother. Int J Clin Pharmacol Biopharm 12: 19-32
Firoz S, Carlson G (2004) Characteristics and treatment outcome of older methadone-maintenance patients. Am J Geriatr Psychiatry 12: 539-41
Fischer B, Rehm J, Brissette S, Brochu S, Bruneau J, El-Guebaly N, Noel L, Tyndall M, Wild C, Mun P, Baliunas D (2005) Illicit opioid use in Canada: comparing social, health, and drug use characteristics of untreated users in five cities (OPICAN study). J Urban Health 82: 250-66
Fricker HS, Segal S (1978) Narcotic addiction, pregnancy, and the newborn. Am J Dis Child 132: 360-6
Friedman R, Kamel I, Perez C, Hamada A (2003) Severe intraoperative hypertension and opioid-resistant postoperative pain in a methadone-treated patient. J Pain 4: 289-90
Gill AC, Oei J, Lewis NL, Younan N, Kennedy I, Lui K (2003) Strabismus in infants of opiate-dependent mothers. Acta Paediatr 92: 379-85
Girela E, Villanueva E, Hernandez-Cueto C, Luna JD (1994) Comparison of the CAGE questionnaire versus some biochemical markers in the diagnosis of alcoholism. Alcohol Alcohol 29: 337-43
Girgis G (2009) Concerns about consensus guidelines for QTc interval screening in methadone treatment. Ann Intern Med 151: 217-8; author reply 218-9
Glatstein MM, Garcia-Bournissen F, Finkelstein Y, Koren G (2008) Methadone exposure during lactation. Can Fam Physician 54: 1689-90
Gossop M, Green L, Phillips G, Bradley B (1989) Lapse, relapse and survival among opiate addicts after treatment. A prospective follow-up study. Br J Psychiatry 154: 348-53
Gossop M, Green L, Phillips G, Bradley B (1990) Factors predicting outcome among opiate addicts after treatment. Br J Clin Psychol 29 (Pt 2): 209-16
Gossop M, Stewart D, Marsden J (2006) Effectiveness of drug and alcohol counseling during methadone treatment: content, frequency, and duration of counseling and association with substance use outcomes. Addiction 101: 404-12

Green L, Gossop M (1988) Effects of information on the opiate withdrawal syndrome. Br J Addict 83: 305-9
Greenwald MK, Schuh KJ, Stine SM (2003) Transferring methadone-maintained outpatients to the buprenorphine sublingual tablet: a preliminary study. Am J Addict 12: 365-74
Grochow L, Sheidler V, Grossman S, Green L, Enterline J (1989) Does intravenous methadone provide longer lasting analgesia than intravenous morphine? A randomized, double-blind study. Pain 38: 151-7
Gunne LM, Gronbladh L (1981) The Swedish methadone maintenance program: a controlled study. Drug Alcohol Depend 7: 249-56
Gutstein, HB and Akil, H. (2006) Opioid Analgesics. In: Goodman and Gilman's Pharmacological Basis of Therapeutics. 11th edition. Brunton L, Lazo JS, and Marker, KI (eds). McGraw-Hill, New York.
Hans SL (1989) Developmental consequences of prenatal exposure to methadone. Ann N Y Acad Sci 562: 195-207
Harding-Pink D (1993) Methadone: one person's maintenance dose is another's poison. Lancet 341: 665-6
Harris KA, Arnsten JH, Litwin AH (2010) Successful Integration of Hepatitis C Evaluation and Treatment Services With Methadone Maintenance. J Addict Med 4: 20-26
Health Canada (2002) Best Practices: Methadone Maintenance Treatment. Minister of Public Works and Government Services, Ottawa
Hillebrand J, Marsden J, Finch E, Strang J (2001) Excessive alcohol consumption and drinking expectations among clients in methadone maintenance. J Subst Abuse Treat 21: 155-60
Hooten WM, Townsend CO, Sletten CD, Bruce BK, Rome JD (2007) Treatment outcomes after multidisciplinary pain rehabilitation with analgesic medication withdrawal for patients with fibromyalgia. Pain Med 8(1):8-16.
Hubbard RL, Craddock SG, Anderson J (2003) Overview of 5-year followup outcomes in the drug abuse treatment outcome studies (DATOS). J Subst Abuse Treat 25: 125-34
Hulse GK, Milne E, English DR, Holman CD (1997) The relationship between maternal use of heroin and methadone and infant birth weight. Addiction 92: 1571-9
Hulse GK, Milne E, English DR, Holman CD (1998) Assessing the relationship between maternal opiate use and neonatal mortality. Addiction 93: 1033-42
Hunt RW, Tzioumi D, Collins E, Jeffery HE (2008) Adverse neurodevelopmental outcome of infants exposed to opiate in-utero. Early Hum Dev 84: 29-35
Iguchi MY, Stitzer ML, Bigelow GE, Liebson IA (1988) Contingency management in methadone maintenance: effects of reinforcing and aversive consequences on illicit polydrug use. Drug Alcohol Depend 22: 1-7
Jansson LM, Dipietro JA, Velez M, Elko A, Knauer H, Kivlighan KT (2009) Maternal methadone dosing schedule and fetal neurobehaviour. J Matern Fetal Neonatal Med 22: 29-35
Jansson LM, Velez M, Harrow C (2004) Methadone maintenance and lactation: a review of the literature and current management guidelines. J Hum Lact 20: 62-71
Jarvis MA, Schnoll SH (1994) Methadone treatment during pregnancy. J Psychoactive Drugs 26: 155-61
Jarvis MA, Wu-Pong S, Kniseley JS, Schnoll SH (1999) Alterations in methadone metabolism during late pregnancy. J Addict Dis 18: 51-61
Jones HE, O'Grady KE, Malfi D, Tuten M (2008) Methadone maintenance vs. methadone taper during pregnancy: maternal and neonatal outcomes. Am J Addict 17: 372-86

Justo D, Gal-Oz A, Paran Y, Goldin Y, Zeltser D (2006) Methadone-associated Torsades de Pointes (polymorphic ventricular tachycardia) in opioid-dependent patients. Addiction 101: 1333-8
Kaltenbach K, Comfort ML (1997) Methadone maintenance of greater than 80 mg during pregnancy. NIDA Research Monograph 174: 128
Kaltenbach K, Finnegan LP (1986) Neonatal abstinence syndrome, pharmacotherapy and developmental outcome. Neurobehav Toxicol Teratol 8: 353-5
Kaltenbach K, Finnegan LP (1987) Perinatal and developmental outcome of infants exposed to methadone in-utero. Neurotoxicol Teratol 9: 311-3
Kaltenback K, Finnegan LP (1992) Methadone maintenance during pregnancy: Implications for perinatal and developmental outcome. In: Sonderegger TB (ed) Perinatal substance abuse: Research findings and clinical implications. Johns Hopkins University Press, Baltimore
Kandall SR, Albin S, Gartner LM, Lee KS, Eidelman A, Lowinson J (1977) The narcotic-dependent mother: fetal and neonatal consequences. Early Hum Dev 1: 159-69
Kandall SR, Doberczak TM, Jantunen M, Stein J (1999) The methadone-maintained pregnancy. Clin Perinatol 26: 173-83
Kanof PD, Aronson MJ, Ness R (1993) Organic mood syndrome associated with detoxification from methadone maintenance. Am J Psychiatry 150: 423-8
Kellogg S, Melia D, Khuri E, Lin A, Ho A, Kreek MJ. Adolescent and young adult heroin patients: drug use and success in methadone maintenance treatment. J Addict Dis. 2006; 25(3): 15-25.
Kienbaum P, Thurauf N, Michel MC, Scherbaum N, Gastpar M, Peters J (1998) Profound increase in epinephrine concentration in plasma and cardiovascular stimulation after mu-opioid receptor blockade in opioid-addicted patients during barbiturate-induced anesthesia for acute detoxification. Anesthesiology 88: 1154-61
King VL, Stoller KB, Hayes M, Umbricht A, Currens M, Kidorf MS, Carter JA, Schwartz R, Brooner RK (2002) A multicenter randomized evaluation of methadone medical maintenance. Drug Alcohol Depend 65: 137-48
Kinlock TW, Gordon MS, Schwartz RP, Fitzgerald TT, O'Grady KE (2009) A randomized clinical trial of methadone maintenance for prisoners: results at 12 months postrelease. J Subst Abuse Treat 37: 277-85
Kletter E (2003) Counseling as an intervention for the cocaine-abusing methadone maintenance patient. J Psychoactive Drugs 35: 271-7
Kraft MK, Rothbard AB, Hadley TR, McLellan AT, Asch DA (1997) Are supplementary services provided during methadone maintenance really cost-effective? Am J Psychiatry 154: 1214-9
Krantz MJ, Martin J, Stimmel B, Mehta D, Haigney MC (2009) QTc interval screening in methadone treatment. Ann Intern Med 150: 387-95
Kreek MJ, Schecter AJ, Gutjahr CL, Hecht M (1980) Methadone use in patients with chronic renal disease. Drug Alcohol Depend 5: 197-205
Lambert M, 1992 Psychotherapy outcome research: Implications for integrative and eclectic therapists. In J.C. Norcross and M.R. Goldfried (Eds.) Handbook of psychotherapy integration. New York: Basic.
Levin FR, Fischman MW, Connerney I, Foltin RW (1997) A protocol to switch high-dose, methadone-maintained subjects to buprenorphine. Am J Addict 6: 105-16
Lewis D, Bellis M (2001) General practice or drug clinic for methadone maintenance? A controlled comparison of treatment outcomes. Int J Drug Policy 12: 81-89
Lifschitz MH, Wilson GS, Smith EO, Desmond MM (1985) Factors affecting head growth and intellectual function in children of drug addicts. Pediatrics 75: 269-74

Ling W, Wesson DR, Charuvastra C, Klett CJ (1996) A controlled trial comparing buprenorphine and methadone maintenance in opioid dependence. Arch Gen Psychiatry 53: 401-7
Little BB, Snell LM, Klein VR, Gilstrap LC, 3rd, Knoll KA, Breckenridge JD (1990) Maternal and fetal effects of heroin addiction during pregnancy. J Reprod Med 35: 159-62
Lovecchio F, Pizon A, Riley B, Sami A, D'Incognito, C (2007) Onset of symptoms after methadone overdose. Am J Emerg Med, 25(1): 57-59.

Lowinson JH, Marion I, Joseph H, Langrod J, Salsitz EA, Payte JT, and Dole VP (2006) Methadone Maintenance. In: Substance Abuse: A Comprehensive Textbook. Fourth edition. Lowinson JH, Ruiz P, Millman RB, and Langrod JG (eds). Lippincott Williams & Wilkins, Philadelphia.
Luty J, Nikolaou V, Bearn J (2003) Is opiate detoxification unsafe in pregnancy? J Subst Abuse Treat 24: 363-7
Maas U, Kattner E, Weingart-Jesse B, Schafer A, Obladen M (1990) Infrequent neonatal opiate withdrawal following maternal methadone detoxification during pregnancy. J Perinat Med 18: 111-8
Magura S, Rosenblum A (2001) Leaving methadone treatment: lessons learned, lessons forgotten, lessons ignored. Mt Sinai J Med 68: 62-74
Man LH, Best D, Gossop M, Stillwell G, Strang J. Relationship between prescribing and risk of opioid overdose among drug users in and out of maintenance treatment. Eur Addict Res. 2004; 10(1): 35-40.
Marsch LA, Bickel WK, Badger GJ, Stothart ME, Quesnel KJ, Stanger C, Brooklyn J (2005) Comparison of pharmacological treatments for opioid-dependent adolescents: a randomized controlled trial. Arch Gen Psychiatry 62: 1157-64
Martin DJ, Garske JP, Davis MK (2000) Relation of the therapeutic alliance with outcome and other variables: a meta-analytic review. J Consult Clin Psychol 68: 438-50
Martin TL, Woodall KL, McLellan BA (2006) Fentanyl-related deaths in Ontario, Canada: toxicological findings and circumstances of death in 112 cases (2002-2004). J Anal Toxicol 30: 603-10
Mason BJ, Kocsis JH, Melia D, Khuri ET, Sweeney J, Wells A, Borg L, Millman RB, Kreek MJ (1998) Psychiatric comorbidity in methadone maintained patients. J Addict Dis 17: 75-89
Mattick RP, Breen C, Kimber J, Davoli M (2009) Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. Cochrane Database Syst Rev: CD002209
Mattick RP, Kimber J, Breen C, Davoli M (2008) Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. Cochrane Database Syst Rev: CD002207
Mayes LC, Carroll KM (1996) Neonatal withdrawal syndrome in infants exposed to cocaine and methadone. Subst Use Misuse 31: 241-53
McCann M, Rawson R, Obert J, Hasson A (1994) A Treatment of Opiate Addiction Using Methadone: A Counselor Manual. Center for Substance Abuse Treatment, Center for Substance Abuse Treatment
McCusker M (2001) Influence of hepatitis C status on alcohol consumption in opiate users in treatment. Addiction 96: 1007-14
McLellan AT, Arndt IO, Metzger DS, Woody GE, O'Brien CP (1993) The effects of psychosocial services in substance abuse treatment. JAMA 269: 1953-9
Mercadante S, Porzio G, Ferrera P, Fulfaro F, Aielli F, Verna L, Villari P, Ficorella C, Gebbia V, Riina S, Casuccio A, Mangione S (2008) Sustained-release oral morphine versus transdermal fentanyl and oral methadone in cancer pain management. Eur J Pain 12: 1040-6

Merrill JO, Jackson TR, Schulman BA, Saxon AJ, Awan A, Kapitan S, Carney M, Brumback LC, Donovan D (2005) Methadone medical maintenance in primary care. An implementation evaluation. J Gen Intern Med 20: 344-9

Mikolaenko I, Robinson CA, Jr., Davis GG (2002) A review of methadone deaths in Jefferson County, Alabama. Am J Forensic Med Pathol 23: 299-304

Milby JB (1988) Methadone maintenance to abstinence. How many make it? J Nerv Ment Dis 176: 409-22

Milby JB, Gurwitch RH, Wiebe DJ, Ling W, McLellan AT, Woody GE (1986) Prevalence and diagnostic reliability of methadone maintenance detoxification fear. Am J Psychiatry 143: 739-43

Murtagh FE, Chai MO, Donohoe P, Edmonds PM, Higginson IJ (2007) The use of opioid analgesia in end-stage renal disease patients managed without dialysis: recommendations for practice. J Pain Palliat Care Pharmacother 21: 5-16

Nelson LB, Ehrlich S, Calhoun JH, Matteucci T, Finnegan LP (1987) Occurrence of strabismus in infants born to drug-dependent women. Am J Dis Child 141: 175-8

Newman RG, Whitehill WB (1979) Double-blind comparison of methadone and placebo maintenance treatments of narcotic addicts in Hong Kong. Lancet 2: 485-8

NIDA (1999) Drug Misuse and DependenceL Guidelines on Clinical Management. National Institute on Drug Abuse Bethesda, MD

Nosyk B, Marsh DC, Sun H, Schechter MT, Anis AH (2010) Trends in methadone maintenance treatment participation, retention, and compliance to dosing guidelines in British Columbia, Canada: 1996-2006. J Subst Abuse Treat 39: 22-31

Novick DM, Kreek MJ, Arns PA, Lau LL, Yancovitz SR, Gelb AM (1985) Effect of severe alcoholic liver disease on the disposition of methadone in maintenance patients. Alcohol Clin Exp Res 9: 349-54

OCP Ontario College of Pharmacists (September 2010). Revised MMT and Dispensing Policy.

Olsen GD, Wendel HA, Livermore, JD, Leger RM, Lynn RK, Gerber N (1977) Clinical effects and pharamcokinetics of racemic methadone and its optical isomers. Clinical Pharmacology & Therapeutics 21(2):147-157.

Ontario Addiction Services Advisory Counsil (2000) Admission and Discharge Criteria for Ontario's Substance Abuse Services. Ontario Substance Abuse Bureau, Ministry of Health and Long-Term Care. Toronto

Ontario Select Committee on Mental Health and Addictions (2010) Final Report Navigating the Journey to Wellness. The Comprehensive Mental Health and Addictions Action Plan for Ontarians. Legislative Assembly of Ontario.

Pani PP, Pirastu R, Ricci A, Gessa GL (1996) Prohibition of take-home dosages: negative consequences on methadone maintenance treatment. Drug Alcohol Depend 41: 81-4

Peles E, Schreiber S, Adelson M. 15-Year survival and retention of pateints in a general hospital-affiliated methadone maintenance treatment (MMT) in Israel. Drug Alcohol Depend. 2010 Mar 1; 107(2-3): 141-8.

Pergolizzi J, Boger RH, Budd K, Dahan A, Erdine S, Hans G, Kress HG, Langford R, Likar R, Raffa RB, Sacerdote P (2008) Opioids and the management of chronic severe pain in the elderly: consensus statement of an International Expert Panel with focus on the six clinically most often used World Health Organization Step III opioids (buprenorphine, fentanyl, hydromorphone, methadone, morphine, oxycodone). Pain Pract 8: 287-313

Perrone J, De Roos F, Jayaraman S, Hollander JE (2001) Drug screening versus history in detection of substance use in ED psychiatric patients. Am J Emerg Med 19: 49-51

Petitjean S, Stohler R, Deglon JJ, Livoti S, Waldvogel D, Uehlinger C, Ladewig D (2001) Double-blind randomized trial of buprenorphine and methadone in opiate dependence. Drug Alcohol Depend 62: 97-104

Pimentel L, Mayo D (2008) Chronic methadone therapy complicated by torsades de pointes: a case report. J Emerg Med 34: 287-90

Polsky D, Glick HA, Yang J, Subramaniam GA, Poole SA, Woody GE (2010) Cost-effectiveness of extended buprenorphine-naloxone treatment for opioid-dependent youth: data from a randomized trial. Addiction 105: 1616-24

Pond SM, Kreek MJ, Tong TG, Raghunath J, Benowitz NL (1985) Altered methadone pharmacokinetics in methadone-maintained pregnant women. J Pharmacol Exp Ther 233: 1-6

Popova S, Rehm J, Fischer B (2006) An overview of illegal opioid use and health services utilization in Canada. Public Health 120: 320-8

Preston KL, Umbricht A, Epstein DH (2002) Abstinence reinforcement maintenance contingency and one-year follow-up. Drug Alcohol Depend 67: 125-37

Rabinowitz J, Cohen H, Tarrasch R, Kotler M (1997) Compliance to naltrexone treatment after ultra-rapid opiate detoxification: an open label naturalistic study. Drug Alcohol Depend 47: 77-86

Rajaratnam R, Sivesind D, Todman M, Roane D, Seewald R (2009) The aging methadone maintenance patient: treatment adjustment, long-term success, and quality of life. J Opioid Manag 5: 27-37

Rauck RL, Bookbinder SA, Bunker TR, Alftine CD, Gershon S, de Jong E, Negro-Vilar A, Ghalie R (2007) A randomized, open-label, multicenter trial comparing once-a-day AVINZA (morphine sulfate extended-release capsules) versus twice-a-day OxyContin (oxycodone hydrochloride controlled-release tablets) for the treatment of chronic, moderate to severe low back pain: improved physical functioning in the ACTION trial. J Opioid Manag 3: 35-43

Rementeria JL, Nunag NN (1973) Narcotic withdrawal in pregnancy: stillbirth incidence with a case report. Am J Obstet Gynecol 116: 1152-6

Repchinsky C (2003) Compendium of Pharmaceuticals and Specialties: The Canadian Drug Reference for Health Professionals. Canadian Pharmacists Association, Ottawa, Ontario

Richman A, Perkins ME, Bihari B, Fishman JJ (1972) Entry into methadone maintenance programs: a follow-up study of New York City heroin users detoxified in 1961-1963. Am J Public Health 62: 1002-7

Ries RK, Dyck DG, Short R, Srebnik D, Snowden M, Comtois KA (2002) Use of case manager ratings and weekly urine toxicology tests among outpatients with dual diagnoses. Psychiatr Serv 53: 764-6

Rosenblum A, Joseph H, Fong C, Kipnis S, Cleland C, Portenoy RK (2003) Prevalence and characteristics of chronic pain among chemically dependent patients in methadone maintenance and residential treatment facilities. JAMA 289: 2370-8

Schmitz JM, Rhoades HM, Elk R, Creson D, Hussein I, Grabowski J (1998) Medication take-home doses and contingency management. Exp Clin Psychopharmacol 6: 162-8

Schottenfeld R, Pakes J, Kosten T. (1998) Prognostic factors in Buprenorpine versus Methadone maintained patients. J Nerv Ment Dis 186(1):35-43.[MEDLINE: 1998118328}

Schreiber S, Peles E, Adelson M (2008) Association between improvement in depression, reduced benzodiazepine (BDZ) abuse, and increased psychotropic medication use in methadone maintenance treatment (MMT) patients. Drug Alcohol Depend 92: 79-85

Schroeder JR, Schmittner JP, Epstein DH, Preston KL (2005) Adverse events among patients in a behavioral treatment trial for heroin and cocaine dependence: effects of age, race, and gender. Drug Alcohol Depend 80: 45-51

Scott CC, Robbins EB, Chen KK (1948) Pharmacological comparison of the optical isomers of methadone. Journal of Pharmacology and Experimental Therapeutics 93:282-286.
Senay EC, Dorus W, Goldberg F, Thornton W (1977) Withdrawal from methadone maintenance. Rate of withdrawal and expectation. Arch Gen Psychiatry 34: 361-7
Sims SA, Snow LA, Porucznik CA (2007) Surveillance of methadone-related adverse drug events using multiple public health data sources. J Biomed Inform 40: 382-9
Sproule B, Brands B, Li S, Catz-Biro L (2009) Changing patterns in opioid addiction: characterizing users of oxycodone and other opioids. Can Fam Physician 55: 68-9, 69 e1-5
Srivastava A, Kahan M (2006) Methadone induction doses: are our current practices safe? J Addict Dis 25: 5-13
Srivastava A, Kahan M, Ross S (2008) The effect of methadone maintenance treatment on alcohol consumption: a systematic review. J Subst Abuse Treat 34: 215-23
Stern R (1966) The pregnant addict. A study of 66 case histories, 1950-1959. Am J Obstet Gynecol 94: 253-7
Stimmel B, Goldberg J, Cohen M, Rotkopf E (1978) Detoxification from methadone maintenance: risk factors associated with relapse to narcotic use. Ann N Y Acad Sci 311: 173-80
Stimmel B, Goldberg J, Reisman A, Murphy RJ, Teets K (1982) Fetal outcome in narcotic-dependent women: the importance of the type of maternal narcotic used. Am J Drug Alcohol Abuse 9: 383-95
Stitzer ML, Iguchi MY, Felch LJ (1992) Contingent take-home incentive: effects on drug use of methadone maintenance patients. J Consult Clin Psychol 60: 927-34
Strain EC, Stitzer ML, Liebson IA, Bigelow GE (1993) Dose-response effects of methadone in the treatment of opioid dependence. Ann Intern Med 119: 23-7
Strike CJ, Gnam W, Urbanoski K, Fischer B, Marsh DC, Millson M (2005) Factors predicting 2-year retention in methadone maintenance treatment for opioid dependence. Addict Behav 30: 1025-8
Subramaniam GA, Fishman MJ, Woody G (2009) Treatment of opioid-dependent adolescents and young adults with buprenorphine. Curr Psychiatry Rep 11: 360-3
Swift RM, Dudley M, DePetrillo P, Camara P, Griffiths W (1989) Altered methadone pharmacokinetics in pregnancy: implications for dosing. J Subst Abuse 1: 453-60
Szabo G, Wands JR, Eken A, Osna NA, Weinman SA, Machida K, Joe Wang H (2010) Alcohol and hepatitis C virus--interactions in immune dysfunctions and liver damage. Alcohol Clin Exp Res 34: 1675-86
Tschakovsky K (2009) Methadone Maintenance Treatment: Best Practices in Case Managment. Centre for Addiction and Mental Health, Toronto
Tuchman E (2007) Exploring the prevalence of menopause symptoms in midlife women in methadone maintenance treatment. Soc Work Health Care 45: 43-62
Tuchman E (2010) Menopause symptom attribution among midlife women in methadone treatment. Soc Work Health Care 49: 53-67
Uhlmann S, Milloy MJ, Kerr T, Zhang R, Guillemi S, Marsh D, Hogg RS, Montaner JS, Wood E (2010) Methadone maintenance therapy promotes initiation of antiretroviral therapy among injection drug users. Addiction 105: 907-13
Unnithan S, Gossop M, Strang J (1992) Factors associated with relapse among opiate addicts in an out-patient detoxification programme. Br J Psychiatry 161: 654-7
Veilleux JC, Colvin PJ, Anderson J, York C, Heinz AJ (2010) A review of opioid dependence treatment: pharmacological and psychosocial interventions to treat opioid addiction. Clin Psychol Rev 30: 155-66

Villano CL, Rosenblum A, Magura S, Fong C (2002) Improving treatment engagement and outcomes for cocaine-using methadone patients. Am J Drug Alcohol Abuse 28: 213-30
Vucinovic M, Roje D, Vucinovic Z, Capkun V, Bucat M, Banovic I (2008) Maternal and neonatal effects of substance abuse during pregnancy: our ten-year experience. Yonsei Med J 49: 705-13
Washton AM, Pottash AC, Gold MS (1984) Naltrexone in addicted business executives and physicians. J Clin Psychiatry 45: 39-41
Wasserman DA, Korcha R, Havassy BE, Hall SM (1999) Detection of illicit opioid and cocaine use in methadone maintenance treatment. Am J Drug Alcohol Abuse 25: 561-71
Wedam EF, Bigelow GE, Johnson RE, Nuzzo PA, Haigney MC (2007) QT-interval effects of methadone, levomethadyl, and buprenorphine in a randomized trial. Arch Intern Med 167: 2469-75
WHO (2009) Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence. World Health Organization, Geneva
Wilson GS, Desmond MM, Wait RB (1981) Follow-up of methadone-treated and untreated narcotic-dependent women and their infants: health, developmental, and social implications. J Pediatr 98: 716-22
Wittmann BK, Segal S (1991) A comparison of the effects of single- and split-dose methadone administration on the fetus: ultrasound evaluation. Int J Addict 26: 213-8
Wolff K (2002) Characterization of methadone overdose: clinical considerations and the scientific evidence. Ther Drug Monit 24: 457-70
Wolff K, Boys A, Rostami-Hodjegan A, Hay A, Raistrick D (2005) Changes to methadone clearance during pregnancy. Eur J Clin Pharmacol 61: 763-8
Wong T, Lee SS (2006) Hepatitis C: a review for primary care physicians. CMAJ 174: 649-59
Woody GE, Poole SA, Subramaniam G, Dugosh K, Bogenschutz M, Abbott P, Patkar A, Publicker M, McCain K, Potter JS, Forman R, Vetter V, McNicholas L, Blaine J, Lynch KG, Fudala P (2008) Extended vs short-term buprenorphine-naloxone for treatment of opioid-addicted youth: a randomized trial. JAMA 300: 2003-11
Yancovitz SR, Des Jarlais DC, Peyser NP, Drew E, Friedmann P, Trigg HL, Robinson JW (1991) A randomized trial of an interim methadone maintenance clinic. Am J Public Health 81: 1185-91
Zador D, Sunjic S (2000) Deaths in methadone maintenance treatment in New South Wales, Australia 1990-1995. Addiction 95: 77-84