CPSNS
Methadone Maintenance Treatment Handbook

COLLEGE OF
PHYSICIANS & SURGEONS
OF NOVA SCOTIA

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1. Introduction

This document has been prepared for the physicians of Nova Scotia as a roadmap for methadone maintenance therapy – that is, the use of methadone primarily as the treatment for opioid dependency.

Overview

As the need for this type of treatment in Nova Scotia is increasing, it is important that the College of Physicians and Surgeons of Nova Scotia (CPSNS or "the College") take a leadership role in establishing standards and best practices in this very complex area of practice. Methadone Maintenance Therapy (MMT) can be both life-saving and fraught with danger. Given that there is a demonstrated need for patients in Nova Scotia to enter into MMT, evidenced by the substantial waitlists for MMT at the major metro and regional methadone clinics, it is clear that the number of Nova Scotia physicians with the knowledge and skills to provide this treatment needs to increase.

This document has been designed to assist both the experienced MMT physician with a focused practice in addiction medicine and the family physician who takes on this role as a component of a busy comprehensive family practice to meet a local need.

This handbook is an adaptation of the College of Physicians and Surgeons of Ontario (CPSO) *Methadone Maintenance Treatment Program Standards and Guidelines* published February 2011. This 4th edition of the CPSO methadone document is the result of many months of work by an expert committee in Ontario, resulting in an essentially new document representing current evidence-based practice standards and guidelines. Our organization is indebted to the CPSO, and in particular Mr. Wade Hillier (Associate Director: Quality Management, CSPO) for giving CPSNS a free hand to use their document as a starting point for ours.

Recognizing that the context of methadone practice in Nova Scotia is different, and taking advantage of the considerable expertise in this province in the use of methadone for treating opioid dependence, an expert committee was established to assist CPSNS in making the needed changes to adapt the CPSO document to our needs. The working group, consisting of Dr. Zac Fraser, Dr. John Fraser, Dr. Ramm Hering, Dr. Sonia Fairfield, Dr. Bill Lowe (Deputy Registrar College of Physicians and Surgeons of Nova Scotia) and Bev Zwicker (Deputy Registrar, Nova Scotia College of Pharmacists) has met regularly to revise this document. Some sections have been adopted with little or no change, some have been adapted with minor or major revisions, and many sections have been entirely rewritten. The College of Physicians and Surgeons of British Columbia (CPSBC) *Methadone Maintenance Handbook* (2006) was also excerpted to form components of many sections. The assistance of Dr. Jack Burak (Deputy Registrar, CPSBC) has been greatly appreciated.

The CPSNS *Methadone Maintenance Treatment Handbook* has been the result of nine months of work by those mentioned above and by many others too numerous to mention. In writing this handbook, the working group has attempted to incorporate evidence-based medicine with best practices gleaned from years of clinical experience. The challenge was to make this handbook relevant to both the experienced MMT prescriber in a focused methadone practice and the family physician with a newly obtained Health Canada exemption for opioid dependence who is responding to the need for more MMT prescribers in rural Nova Scotia.

The authors of this document have attempted to develop statements representing both standard of practice ("Standards") and best practice ("Guidelines") for MMT physicians. Clearly, individual variation in practice exists and is appropriate where supported by evidence and sound medical judgement. Efforts have been made to distinguish between statements that represent a standard of care – carrying CPSNS's expectation that members comply – and best practice, which is seen as the recommended action – subject to the clinical context and the clinical judgement of the provider.

1.1 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, Bayer developed methadone, a long-acting pure mμ agonist, as an analgesic in Germany. 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, opioid use became a serious concern in urban areas, resulting in 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, Drs. Dole and Nyswander performed the first methadone study at The Rockefeller Institute for Medical Research in an attempt to develop a new pharmacotherapy for opiate dependence.[1-2]

Their research concluded that methadone prevented opioid withdrawal symptoms, blocked the euphoria of heroin, and decreased cravings in opioid-dependent individuals, thereby confirming that methadone was an efficacious 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 world's first MMT program.[3] 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.[4] 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.[5] Between 1990 and 1994, there was a significant rise in individuals addicted to controlled-release oxycodone seeking treatment at the Centre for Addiction and Mental Health (CAMH).[6] A chart review of CAMH's new MMT admissions (1997-99) also revealed that 83% of patients had used prescription opioids with or without heroin. The semi-synthetic oxycodone and full-synthetic fentanyl have been linked to several deaths in Ontario.[7-8] Experience in Nova Scotia suggests that the abuse of prescription opioids such as oxycodone (Oxycontin) and hydromorphone (Dilaudid) predominates in the population requiring treatment for opioid dependence.

Literature on the effectiveness of MMT in the treatment of prescription opioid addiction is sparse. Banta-Green, et al. reported that prescription opioid users could be treated at least as effectively as heroin users in MMT.[9] 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.[10]

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 for "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 others involved in treatment.

Although methadone alone is an effective treatment of opioid dependency, outcomes with MMT are improved with the addition of addiction counselling and support services.

Effective MMT services should include the following components:

1. Routine medical care
2. Treatment for other substance dependencies
3. Counselling and support
4. Mental health services
5. Education, health promotion, and disease prevention
6. Linkages to other community-based services
7. Outreach and advocacy

1.2 Effectiveness of Methadone

Methadone has been extensively researched for safety and its efficacy to reduce morbidity and mortality in heroin-dependent patients.

MMT reduces morbidity and mortality associated with heroin addiction.[11-13] ***One study found that patients were three times more likely to die without MMT than if they were maintained on treatment.***[14]

In addition, studies have shown that MMT can indirectly decrease mortality by decreasing the risk of HIV infection while on MMT.[15-16] A Cochrane review[17] 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. [11-12, 18] For example, an early trial found that compared to methadone, the control group was more than three times more likely to test positive for heroin use at a one-month follow-up after treatment.[18] MMT also reduces other substance use. One large prospective study[19] 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 counselling, adequate dosing, contingency management strategies (such as take-home doses), and harm reduction program orientation.[20-25]

There are still few studies on the effectiveness of MMT for prescription opioid abuse and dependence.

1.3 Pharmacology of Methadone

Methadone has ideal pharmacologic properties for a maintenance agent. Methadone is an oral long-acting synthetic opioid that effectively treats opioid dependence. It is primarily a mu (μ) opioid receptor agonist, and when administered in an appropriate dose, it will prevent opioid withdrawal, reduce opioid craving and block the euphoric effects of other opioids without producing euphoria or sedation. This enables patients to function normally (i.e, without impairment), and experience normal pain and emotional responses.

Knowledge of the pharmacology of methadone is important and will assist practitioners in avoiding problems associated with overdosing or relapse due to underdosing.

There is significant inter-individual variability in the pharmacology of methadone. The oral methadone dose required to achieve a plasma concentration of 250 ug/ml in 70 kg patients (on no other medications), ranged from 55-921 mg a day.[26] Methadone demonstrates incomplete and unpredictable cross-tolerance with other opioids.

The combination of inter-individual variability in methadone pharmacology and incomplete cross-tolerance with other opioids makes determining equianalgesic doses and predicting doses required to prevent opioid withdrawal very difficult, if not impossible.

1.3.1 Bioavailability

Oral methadone is 80% bioavailable with a range of 36-100%. It is rapidly absorbed into plasma in 15 to 45 minutes. The peak plasma concentration and peak clinical effect occurs in 2.5 to 4 hours.

1.3.2 Distribution

Methadone has high lipid solubility and is 86% protein bound (range 81-97%).[27] It is transported across the blood brain barrier efficiently, resulting in CSF concentrations, which are 73% of serum concentrations.

Methadone is present in breast milk, with infant exposure at 2.8% of the maternal dose. Methadone crosses the placenta and may cause physical dependency resulting in neonatal abstinence syndrome.[28]

1.3.3 Metabolism

Methadone is extensively metabolized in the liver to pyrrolidines and pyrroline (via *N*-demethylation and cyclization), which are then excreted in urine and bile.[29] Methadone metabolism is primarily a function of liver enzyme activity involving cytochrome P450 isoenzymes. The major isoenzyme involved is CYP-3A4, which has a 30-fold variable expression. There are many drugs that interact by inducing or inhibiting CYP-3A4 activity (See Appendix A: Drug to Drug Interactions). This can result in clinically significant changes in methadone activity. Genetic and environmental factors can also act on these enzymes leading to a high degree of variation of individual methadone responsiveness. Methadone has no active metabolites.[30]

1.3.4 Elimination

Methadone has an extremely variable plasma half-life – averaging 24 to 36 hours but ranging from 4 to 90 hours. There is a 20-fold inter-individual variability in the plasma half-life. The clearance of methadone increases with chronic dosing, and the plasma half-life may be as long as 55 hours at the start of treatment, decreasing to 24 hours with chronic treatment. It takes about 5 days for methadone plasma levels to reach steady state.[31]

As a result of its long half-life, methadone may accumulate leading to sedation and respiratory depression. This is particularly significant at the start of treatment when the half-life may be longer. As a result, dose increases need to occur slowly allowing the plasma levels to reach steady state before a further dose increase.[31]

With those infrequent patients in whom the methadone plasma half-life is less than 20 hours ("rapid metabolizers"), daily methadone dosing might not be sufficient to adequately prevent withdrawal symptoms for 24 hours. In these cases, twice daily dosing may be required.

Methadone has a biphasic elimination. The α-elimination phase (8 to 12 hours) correlates with the analgesic effects, and the β-elimination phase (30 to 60 hours) correlates with plasma levels, which are subanalgesic but sufficient to prevent withdrawal. As a result, although methadone can be dosed once a day for opioid

addiction, it usually has to be dosed 2 or 3 times a day for analgesia.[27]

Methadone is primarily excreted by the fecal route. There is little urinary elimination and methadone levels are not affected by renal insufficiency.[27]

1.3.5 Tolerance

Cross-tolerance between methadone and other opioids is unpredictable. The rate of development of tolerance varies between individuals.

Tolerance to the various effects of methadone develops at different rates. Tolerance to the euphoric effects develops quickly and may be interpreted by patients as being due to an inadequate dose. Tolerance to respiratory depression is less rapid in onset, and tolerance to the autonomic side effects is the slowest. Tolerance can rapidly be lost upon stopping methadone in as little as 3 days.

1.4 Professional Duties

MMT physicians are responsible for the following:

1. Providing professional, respectful, non-judgmental and reliable services to patients
2. Providing back-up coverage for periods when on vacation or otherwise unavailable
3. Providing appropriate notice should they close their MMT practice
4. Assisting in the transfer of patients to other MMT physicians
5. Providing or facilitating patient access to health and social services, such as counselling and primary health care
6. Remaining current in practices and standards for MMT and the treatment of opioid dependence and other addictions
7. Communicating and collaborating with pharmacists and other care providers for the benefit of the patient

1.5 Inter-Professional Collaboration (IPC)

1.5.1 Physician-Pharmacist Collaboration and Communication

Evidence shows that lack of communication between MMT prescribers and pharmacists has been the direct cause of many problems in patient care.[32]

To optimize patient care, communication between physicians and pharmacists is essential in the following:

1. Determining at the outset of treatment whether a pharmacy is accepting new patients
2. Discussing how and when the pharmacist is to contact the MMT prescriber
3. Developing means for the pharmacist to reach the MMT prescribe after hours for urgent issues
4. Documenting or relaying pertinent clinical information (e.g., pregnancy, missed doses, vomited doses, etc.)

Inter-professional collaboration is a principle supported by both CPSNS and the Nova Scotia College of Pharmacists (NSCP). The pharmacist and the physician play an important role in MMT. This can include joint development of policies and procedures to ensure continuity of patient care and secure custody and storage of methadone. Collaboration and regular communication between pharmacists and MMT prescribers can have positive impact on patient care and safety (See Appendix B: Sample Physician Pharmacist Treatment Agreement Letter).

1.6 Conclusion

MMT saves lives and reduces violent and non-violent crime, drug use, and the transmission of HIV, Hepatitis C, and other communicable diseases.

The medical literature supports that MMT is a well-established and cost-effective treatment paradigm. The effectiveness of MMT is enhanced with contingency management and counselling.

2. MMT Physicians and Practice Settings

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

Overview

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

STANDARDS

1. The MMT physician shall successfully complete the CAMH *Opioid Dependence Treatment Core Course* for opioid dependency (or the equivalent at the discretion of the Registrar) prior to obtaining a methadone exemption.
2. The MMT physician shall complete one day of clinical training with a MMT physician approved by the CPSNS.

GUIDELINES

1. It is suggested that MMT prescribers should successfully complete the full Opioid Dependence Certificate Program within 3 years of receiving an exemption.

There are two classes of Health Canada exemptions allowing licensed physicians to prescribe methadone in Canada – one for analgesia and one for dependence. Both exemptions are granted by Health Canada on the recommendation of the appropriate medical regulatory authority.

The usual requirement for analgesia exemption is in chronic pain cases where patients have been resistant to other measures. Such physicians are advised to be familiar with the following CPSNS documents:

- Guidelines for the Use of Controlled Substances in the Treatment of Pain (download PDF)
- Guidelines for Methadone in the Management of Chronic Non-Cancer Pain (download PDF)
- Canadian Guidelines for the Safe and Effective Use of Opioids for Chronic Non-Cancer Pain

Many Nova Scotia physicians with exemptions for the use of methadone in analgesia have obtained the exemption for use in the care of a single patient with chronic pain. In such situations, the decision to initiate methadone for chronic pain is often made in consultation with a pain specialist.

A recommendation to Health Canada for approval of the exemption allowing physicians to prescribe methadone for dependence requires approval by the CPSNS Methadone Program as part of the Health Canada application process. Approval of the exemption application requires that the physician be a licenced member of CPSNS and be in good standing with the College. In the case of requests for approval of exemptions for opioid dependence, the physician must also demonstrate adequate knowledge of MMT and addiction medicine (See Section 2.1 Obtaining a Methadone Exemption).

2.1 Obtaining a Methadone Exemption

For an exemption to prescribe MMT, a physician must:

1. Hold a license to practice medicine in Nova Scotia-
2. Be in good standing with the CPSNS
3. Complete an application form and agree to practice in accordance with the *CPSNS Methadone Maintenance Treatment Handbook*
4. Successfully complete the *Opioid Dependence Treatment Core Course* through CAMH
5. Complete one day of clinical training with a MMT physician approved by the CPSNS

The initial exemption is issued for one year, with subsequent exemptions issued every three years. For more information contact the CPSNS Methadone Program: (902) 421-2216. The above conditions must be met in entirety for CPSNS to support a College member's application to Health Canada for a methadone exemption for dependency. Contact Health Canada to obtain an application form (See Appendix C: Resources).

2.2 MMT Physician Practice Settings

2.2.1 Primary Care MMT Practice

General practitioners and family physicians may provide MMT in solo medical practice or group practices such as private medical clinics, hospital-based health clinics and community-based health centers, including chronic care centers. Methadone prescription may be integrated with the physician's medical practice or separate from it. Some MMT patients in Nova Scotia 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.[33-36] However, patients may be required to travel to receive pharmacy, laboratory, and other specialized addiction and support services.

Group practices may have advantages over solo practice.

Research 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.[37]

2.2.2 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 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. Methadone prescribers may have a separate practice, but may not have the capacity to provide primary care services to MMT patients. Patients may need to seek out primary care or psychosocial services in the community. In situations where the patient does not have immediate access to primary care, the MMT prescriber is encouraged to provide critical primary care until the patient obtains a primary care provider.

2.2.3 Community-Based MMT Practice

Community-based physicians may provide services through publicly funded, community-based clinics that integrate psychosocial care. Examples include HIV/AIDS services, mental health agencies, and clinics run by local public health departments.

These clinics often specialize in serving specific populations or issues such as HIV/AIDS, Hepatitis C, and marginalized, street-involved or homeless populations. Many community-based clinics operate under a "harm-reduction" philosophy and involve a multi-disciplinary team in the patient's care (i.e., social workers, nurses, case managers, dieticians, pharmacists).

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

2.2.4 Hospital and Corrections-Based MMT Practice

MMT physicians in hospitals, and some residential addiction treatment centres, 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 14. Hospital-Based MMT).

Correctional facilities manage many patients with opioid dependence and should 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.

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.

STANDARDS

1. The MMT physician shall inform the patient of all the treatment options to treat opioid dependence, including risks and benefits, so they 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*. In order to prescribe buprenorphine a methadone exemption for opioid dependence is required.

GUIDELINES

1. It is recommended that physicians planning to prescribe buprenorphine should also complete the online buprenorphine CME course or equivalent.
2. The MMT physician should be familiar with the individual patient factors to be taken into consideration in the choice of buprenorphine as an opioid agonist therapy.

3.1 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 (i.e., AA, CA, NA). While abstinence-based treatment is less effective than MMT, patients may prefer a trial of abstinence before committing to long-term opioid agonist therapy.[38]

Experience in Nova Scotia 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.

According to a 2009 Cochrane Database review of MMT, methadone is an effective maintenance therapy intervention for the treatment of heroin dependence as it retains patients in treatment and decreases heroin use better than treatments that do not utilise opioid replacement therapy.[17]

Patients should be warned that after detoxification:

1. Their tolerance to opioids will go down, putting them at risk for overdose if they relapse to their usual opioid dose.

2. The emotional distress associated with opioid withdrawal may increase the risk of suicidal ideation.

MMT physicians should take appropriate precautions to avoid these adverse outcomes.

3.1.1 Indications for Abstinence-Based Treatment

The following factors should be considered when determining the appropriateness of 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).[39-43]

3.1.2 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). 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 orally, twice daily to three times daily	Agitation, diaphoresis, and sympathetic overdrive
Dimenhydrinate	50 mg orally or rectally as needed	Nausea
Ibuprofen	200 mg 1-3 tabs orally, three times a day as needed	Myalgia
Immodium	2 mg orally as needed (maximum 6 tabs a day)	Diarrhea stool

Drug	Dose	Opioid Withdrawal Symptoms
Trazodone	50-100 mg orally at night as needed	Insomnia
Benzodiazepines	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 about mixing with opioids, or having prolonged hot bath (both can cause hypotension).
4. Don't prescribe for longer than 2 weeks (rebound hypertension).

3.2 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** Guidelines PDF here
> **Visit website:** www.knowledgex.camh.net/primary_care/guidelines_materials/Documents/buprenorphine_naloxone_gdlns2011.pdf

Please note: Must first logon to CAMH website to access download

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. [44-45] ***However, buprenorphine may also be somewhat less effective than methadone at retaining patients in treatment.*** [45]

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.[46-48] MMT is considered first-line therapy.

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[49-50]
- Patients who are unable to tolerate methadone
- Patients who have failed methadone maintenance treatment

3.2.1 Buprenorphine: Practical Issues

As with other opioids, buprenorphine is subject to the federal Controlled Drugs and Substances Act and buprenorphine prescriptions are monitored by the Nova Scotia Prescription Monitoring Program (NSPMP).

Access to buprenorphine may be limited for some patients due to restrictions of payers (e.g., provincial formulary for Nova Scotia Pharmacare, Non-Insured Health Benefits (NIHB) Program, etc.).

4. Initial Patient Assessment

Initially assessing a patients' suitability for MMT includes several important first steps.

Overview

Initially assessing a patients' suitability for MMT includes several important first steps. An initial assessment for MMT involves assessing the patient's suitability for MMT, reviewing their documented history, and conducting a focused physical examination (including urine drug screening and other investigations), followed by a discussion and review of treatment options and necessary documents pertinent to MMT.

STANDARDS

1. The MMT physician shall establish that the patient meets the DSM IV criteria for opioid dependence prior to MMT initiation (See Appendix D: 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 MMT initiation (i.e., discussing side effects, risks, and difficulty withdrawing and tapering off of methadone).
4. The MMT physician shall obtain a patient profile for the previous 12 months through the Nova Scotia Prescription Monitoring Program (NSPMP) and shall register the patient in the NSPMP Methadone Program Monitoring Service.

GUIDELINES

1. The MMT physician should consider abstinence-based treatment and/or opioid substitution for withdrawal purposes for patients whose duration of opioid dependence is less than 1 year.
2. The MMT physician should consider MMT for patients after a thorough assessment and discussion about all treatment options.
3. The MMT physician should take more caution with patients under 18 years of age. A second opinion, with an experienced methadone provider should be sought prior to initiating a patient less than 18 years of age on MMT.
4. For all patients that may be initiated on MMT, the physician should document the following:
   a. General history
   b. Addictions history – including detailed substance use and treatment history, and high-risk behaviour history
   c. Medical history (including cardiovascular history, chronic pain history and blood borne pathogen history)
   d. Psychiatric history (current and past including suicidal ideation)
   e. Social history (including legal, housing, child custody and the partner's drug use history)
5. The MMT physician should conduct a focused physical examination prior to initiating MMT or within a reasonable amount of time (i.e., during the early induction phase).
6. If an initial UDS is positive for EDDP, the MMT physician should verify the source of methadone with the patient (such as non-prescribed or obtained by prescription in another province).
7. The MMT physician should request blood work serology (screening for HIV, and Hepatitis A, B and C) during initiation or within a reasonable amount of time after initiation on MMT.

8. The MMT physician should test for pregnancy in female patients of childbearing potential prior to initiating MMT.
9. All physicians who wish to prescribe methadone should apply for eAccess through the Nova Scotia Prescription Monitoring Program.
10. The MMT physician should have a written Treatment Agreement signed by the patient and documented in the chart (See Appendix E: Sample Methadone Maintenance Treatment Agreement and Section 4.1 Criteria for MMT).

4.1 Criteria for MMT

The MMT physician should only consider MMT for patients after a thorough assessment and discussion about all treatment options.

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)
2. Meets DSM IV criteria for opioid dependence (See Appendix D: Diagnostic Criteria for Substance Dependence)
3. No contraindications to MMT
4. Agreement to terms and conditions of the MMT program

TABLE 02: 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.

4.1.1 Adolescents

Patients under 18 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 treatment options has taken place. The MMT physician should ensure that there has been 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/or may request a consultation with an experienced MMT physician.

4.2 Assessing a Patient for MMT Initiation

There are a number of important areas to consider with regards to patient history for this population of patients (See Appendix F: Sample Initial Patient Assessment Form).

4.2.1 General History

- Any relevant current or past medical history
- Current or past medication use including non-prescription products,
- Current or past hospitalizations and surgeries

4.2.2 Addictions History

- Ensure the patient meets the DSM IV criteria for opioid dependence prior to MMT initiation
- Identify any potential risks for methadone toxicity prior to MMT initiation (See Table 04: Patient Factors that Increase Risk of Methadone Toxicity[67-68])
- Pattern of use of all major drug classes (including tobacco and alcohol)
- Previous addiction treatment history and response
- High-risk behaviour such as needle sharing, commercial sex work and driving while intoxicated
- Screening for behavioural addictions (See Appendix G: Behavioural Addictions)

4.2.3 Medical History

4.2.3.1 Cardiovascular History

Careful screening for the risk of cardiac conduction abnormalities must be performed.

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[51-55] (See Appendix H: Medications that Cause Prolonged QTc Interval)

While it seems to be dose-dependent, it is important to note that sudden cardiac death associated with methadone has been seen at dosages as low as 29 mg a day.

This means that arrhythmia can occur in dosages commonly used to treat addiction, and that dosage is just one consideration with regard to limiting arrhythmia risk.[56] That said, high methadone doses have been associated with prolonged QTc interval, which can cause Torsades de Pointes (a ventricular arrhythmia).[51,57] 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.[58]

4.2.3.2 Chronic or Recurrent Pain

Past illness or injury resulting in chronic pain

4.2.3.3 Blood-Borne Pathogens

History of serological testing for HIV, Hepatitis C and immunity to Hepatitis A and B

4.2.4 Psychiatric History

Current and past psychiatric history and current mental status including suicidal ideation

4.2.5 Social History

Social situation including housing, supports, child custody, legal problems, financial stability and partners drug-use history

4.2.6 Focused Physical Examination

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

4.2.7 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. See Section 6. Urine Drug Screening (UDS) for additional information.

4.2.7.1 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:

a. The patient has signs and symptoms of obvious opioid withdrawal **OR**
b. The patient has obvious track marks **OR**
c. The patient has been on previous MMT (discuss inconsistency with patient)

The MMT physician shall:

1. Obtain corroborating information from a previous opioid prescribing physician and/or reliable agencies as well as NSPMP patient profile
2. Consult with an experienced methadone maintenance prescriber if information is unavailable

4.2.7.2 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 EDDP (a methadone metabolite), it is important to document the patient's history of methadone use.

To avoid MMT duplication and toxicity, the MMT physician must obtain a patient drug profile from NSPMP to ensure that the patient is not on another MMT program.

4.2.8 Other Tests

In addition to UDS, the MMT physician should request appropriate screening blood work for HIV, Hepatitis A and B,[I] Hepatitis C, and RPR/VDRL during initiation or within a reasonable amount of time after initiation on MMT. In females of childbearing potential, a urine pregnancy test should be done prior to initiating MMT. Other relevant blood work[II] can be ordered as indicated. Occasionally, patients refuse or will not comply with this directive. The MMT physician should discuss the concerns with the patient and document the discussion.

I To determine the status of immunity to hepatitis A and B
II Other relevant blood work should include BUN, creatinine, electrolytes, ALT, AST, GGT, ALP, serum albumin, and INR

4.3 MMT Program Documentation

4.3.1 The Nova Scotia Prescription Monitoring Program (NSPMP)

Patients may not receive a prescription for methadone from more than one source at a time. For this reason, prior to initiating treatment, the MMT physician must contact NSPMP.

A current patient profile must be obtained and the patient must be enrolled in the NSPMP Methadone Program Monitoring Service. A current patient profile can be obtained either through the NSPMP eAccess web application or by contacting NSPMP directly. This service will provide the physician with a patient drug profile prior to initiating treatment. Also, NSPMP conducts weekly monitoring of patient profiles and advises physicians if the patient has obtained a monitored drug from other prescribers during the course of their treatment.

4.3.2 Treatment Agreement

Written Treatment Agreements (or Letters of Understanding) 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 documentation of informed consent (See Appendix E: Sample Methadone Maintenance Treatment Agreement).

A treatment agreement should include:

1. Patient and provider roles and responsibilities
2. MMT program expectations and structure
3. Doctor-patient confidentiality and exceptions to this
4. Expectations of communication with other appropriate providers (i.e., pharmacist, treating primary care physicians and consultants)
5. Descriptions of risks and benefits to patient
6. General consent (e.g., access to patient charts for MMT quality improvement peer review of their MMT practice)

It is recommended that the MMT physician communicate his/her expectations with the pharmacist at pharmacies where their patient's methadone is dispensed. This can be accomplished through **one** of the following:

a. A letter to the pharmacist outlining details of the treatment agreement along with expectations regarding missed doses or intoxication. This may also include the MMT physician's contact information in case of emergency (See Appendix B: Sample Physician Pharmacist Treatment Agreement Letter) **OR**
b. 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 or intoxication. It may also include communicating the MMT physician's contact information in case of emergency.

Pharmacists provide methadone to patients with substance dependence in accordance with the Standards of Practice adopted by the Nova Scotia College of Pharmacists (NSCP). These standards align well with this document, and physicians can refer pharmacists to their standards posted on the NSCP website as needed.

5. Dosing During Induction, Stabilization and Maintenance

Patients are at a high risk of death from methadone overdose in the first 2 weeks of MMT.

Overview

Patients are at a high risk of death from methadone overdose in the first 2 weeks of MMT. Recent prospective population studies from the UK and Australia have revealed that during the first 2 weeks of methadone treatment the crude mortality rate was 17 per 1000 person years.[59-60]

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.[61] A single day's MMT dose can be lethal to non-tolerant individuals.[62] The ratio between the maximum recommended initial dose (30 mg) and a potentially fatal single dose is exceedingly narrow compared to other medications.[63-64]

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 1 can be toxic by days 3 to 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 lability.[65]

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.[66]

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

Stage 1: *Induction*: the initial period of MMT (less than 60 mg daily) when the dose is increased safely but rapidly enough to minimize significant withdrawal symptoms

Stage 2: *Stabilization*: period during which the stable dose is being approached (usually 60 mg and above)

Stage 3: *Maintenance*: when a stable dose has been reached

STANDARDS

1. On the methadone prescription, the MMT physician shall specify:
   a. The total quantity of methadone written in numbers and words
   b. The daily dose mixed in Orange Tang or other crystalline juice to a consistent final volume (100 ml recommended)
   c. The days of the week that require witnessed ingestion
   d. Number of take-home doses authorized (when applicable)
   e. Start and end dates
2. During the induction, the MMT physician shall counsel the patient on strategies to minimize risks associated with methadone (including explaining the risks of diverted methadone).

3. During the induction, the MMT physician shall ensure the reasons for all dosage adjustments are documented and should ensure doses are only increased after the patient has been assessed in-person, and it is determined that the patient is experiencing cravings and a constellation of withdrawal symptoms and/or ongoing opioid use.
4. During the induction, the MMT physician shall ensure that the starting methadone dose for all patients is 30 mg or less.
5. During the induction, the MMT physician shall ensure that the starting methadone dose for patients at higher risk for methadone toxicity is 20 mg or less.
6. During the induction, the MMT physician shall ensure that the initial methadone dose during induction for new MMT patients who have been abstinent from opioids for 7 or more days is 10 mg or less.
7. During the induction, the MMT physician shall assess the patient before each dose increase if possible during induction and in-person at least weekly.
8. During the induction, if lack of access to the MMT physician significantly increases the risk of patient withdrawal from treatment, a regulated non-physician health care provider may be formally delegated under a Delegated Medical Function (DMF) to provide clinical assessments prior to each dose increase during induction.[III]
9. During the induction, for patients who are not at higher risk for methadone toxicity, the MMT physician shall prescribe dose increases of no more than 10 mg every 3 days or 15 mg every 5 days during the induction phase and 10 mg every 5 days (7 days recommended) during the stabilization phase.
10. During the induction, for patients at higher risk of methadone toxicity, the MMT physician shall prescribe dose increases of no more than 5-10 mg every 5 days during the induction phase and 5-10 mg every 5 days (7 days recommended) during the stabilization phase.
11. During the induction, for patients who have recently been abstinent from opioids for 7 or more days, the MMT physician shall prescribe dose increases of no more than 5 mg every 3 to 5 days during the induction phase and 5-10 mg every 5 days (7 days recommended) during the stabilization phase.
12. During the stabilization phase, when the patient's dose of methadone is still changing, the MMT physician shall see and assess the patient prior to each dose increase. The MMT physician shall increase the dose by no more than 10 mg every 5 days (7 days recommended), depending on the patient's cravings, opioid use, withdrawal symptoms, and underlying risk for toxicity.
13. During the maintenance phase, if a patient has missed methadone doses for 10 days or less, the MMT physician may restabilize the patient up to their previous maintenance dose at a more rapid rate than specified in Standard 12 (above). In-person assessment by the MMT physician for each dosage increase during such restabilization is not necessary provided that the dose increase is being supervised by a delegated provider in direct communication with the MMT physician (See Guidelines 6-8, Section 5: Dosing During Induction, Stabilization and Maintenance).
14. During the maintenance phase, the MMT physician shall order an ECG with a calculated QTc interval for patients at a dose of 150 mg and then again after every 30-50 mg dose increase.

GUIDELINES

1. During induction, the MMT physician should avoid prescribing any sedating drugs. The MMT physician should also advise the patient to avoid any new sedating medications or drugs.
2. During the induction phase, if the patient misses one dose during the induction phase, the same dose may be repeated and the dose should not be increased to the next dose level until 3 total doses and 2 consecutive doses have been given.

III The physician, and the provider to whom this function will be delegated within a health authority facility, must apply to the District Health Authority ((DMAC)) for approval of a specific DMF where a non-physician can be substituted for a delegating physician under certain conditions. To delegate a medical function to a non-physician provider in a private facility or physician's office, the application for approval must go to their respective provincial regulatory authorities. According to a formally approved DMF the delegating physician retains some overall accountability, but the non-physician provider may perform the function independently according to a written protocol (See the CPSNS policy on Delegated Medical Functions: www.cpsns.ns.ca/PhysicianGuidelinesandPolicies.aspx?EntryId=20). The College of Registered Nurses of Nova Scotia (CRNNS) has a similar policy. An explanation of recent changes to the DMF process is available on the CRNNS website: www.crnns.ca/default.asp?id=190&sfield=content.id&search=4572&mn=414.1116.1124.1712.254

3. During the induction phase, if the patient misses 2 consecutive daily doses during the induction phase, and the 2 days occur before the patient has completed 3 total doses at a dosage level, the dose should return to the previous dosage level for a minimum of 2 consecutive days before increasing to the current dosage again.
4. During the induction phase, if the patient misses 2 consecutive daily doses during the induction phase and the 2 missed days are immediately after completing 3 consecutive doses at a dosage level, they should receive another 2 consecutive doses at the last given dosage level before increasing to the next dosage level.
5. During the induction phase, if the patient misses 3 or more consecutive doses during the induction phase, the MMT physician or pharmacist shall cancel all subsequent doses. The MMT physician should assess the patient in-person, and restart the patient at 30 mg or less maintaining this dose for at least 3 consecutive days.
6. During the stabilization phase, the MMT physician shall reduce the dose by 50% or to a dose of 50 mg (whichever is higher) when a patient has missed 3 to 5 consecutive daily doses during the stabilization or maintenance phases. The dose can then be increased by 10-15 mg every 1 to 3 days (see 5.6.2 Missed Doses During Stabilization Phase) until the patient's original maximum dose is reached.
7. If the patient misses 6 to 10 consecutive daily doses of methadone during the stabilization or maintenance phases, the MMT physician shall reduce the dose to 30 mg or less. The dose then can be increased by no more than 10 mg every 2 days up to 60 mg a day, and then increased by 10 to 15 mg a day every 3 to 5 days until the patient's original dose is reached. (see 5.6.2 Missed Doses During Stabilization Phase)
8. During the stabilization phase, the MMT physician shall restart methadone according to the induction protocol when a patient has missed 11 or more consecutive daily doses of methadone (See Standards 4-11, Section 5: Dosing During Induction, Stabilization and Maintenance).
9. During the induction phase, 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 initiation (as small a dose as is safely possible to avoid withdrawal), preferably in a supervised setting in consultation with an addiction medicine physician.
10. During the maintenance phase, the MMT physician should assess patients weekly to monthly based on the recovery needs of the patient.
11. The MMT physician should identify and manage risk factors for increased QTC and Torsades de Pointes arrhythmias, and should obtain an ECG at time of induction for patients with these risk factors.
12. During the maintenance phase, the MMT physician should consider reducing or tapering the dose of methadone if the patient reports sedation or other cognitive effects in the stabilization and maintenance phases.
13. During the maintenance phase, when considering a patient for a dose increase, the MMT physician should assess the patient for other conditions that are commonly confused with withdrawal symptoms.
14. If the patient has emesis after taking methadone, the MMT physician should only replace the dose if the emesis was witnessed by the pharmacist or staff and it occurred less than 30 minutes after consumption. The replacement dose is generally no more than 75% of the original dose if the emesis occurred within 15 minutes of the dose being taken, and no more than 50% of the regular dose if the emesis occurred within 15 to 30 minutes of the regular methadone dose being taken.
15. Consideration should be given to replacing vomited doses for pregnant patients even if not witnessed.

5.1 Writing a Methadone Prescription

Safe dispensing of methadone begins with a well-written prescription. All prescriptions for methadone must be written on NSPMP duplicate prescription pad. Collaboration and communication between the physician and the pharmacist help to enhance patient safety (See Appendix I: Sample Methadone Prescriptions).

On the methadone prescription, the MMT physician shall specify:

1. The total quantity of methadone in milligrams for the entire duration of the prescription, written in numbers and words (to help prevent tampering of prescriptions)
2. The daily dose mixed in Orange Tang or other crystalline juice (the recommended final volume is 100 ml. This is consistent with the NSCP Standards of Practice for pharmacists, which includes a standardized 100 ml end volume to minimize compounding errors, to standardize the taste of a patient's dose, and for consistency with practice in most of the other provinces. Patients unable to tolerate the ingestion of 100 ml should receive their daily dose in a final volume of 50 ml. Patients pending surgery for any reason or "nothing by mouth" patients (NPO) should receive their daily dose in a final volume of 15 ml.)
3. The days of the week that require witnessed ingestion
4. The start and end date (same as standard #1)
5. The number of take-home doses (or "carries") per week if applicable

5.2 Strategies to Reduce Risks of Methadone

Methadone has demonstrated itself to be a substance with the potential to provide significant benefit as well as the potential to cause significant harm. The following should be practiced to optimize the benefits while minimizing the risks:

Patient Education

Explain to the patient that it takes several weeks to reach the optimal dose of methadone, and that it is dangerous to try to relieve withdrawal symptoms with benzodiazepines or other opioids (including additional illicitly obtained methadone).

Advise the patient to:

1. Limit his or her driving or use of machinery after a dose increase, particularly in the first few hours after dosing.
2. Take the methadone dose in the morning during induction and stabilization, since the risk of overdose is increased if it is consumed prior to sleeping.[64]

Explain the risks of diverted methadone:

1. A single dose of methadone can be fatal.
2. Patients are responsible for the safe storage of their methadone.

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 to help explain the risks of and how to avoid methadone toxicity (See Appendix J: Patient Guide on Methadone Overdose).

Frequency of Visits

Schedule patient visits at least once weekly during induction and with dose changes during stabilization. However, twice-weekly visits during the first 2 weeks of treatment are recommended, particularly if the patient is at increased risk for methadone toxicity. The physician should inquire about sedation and other side effects at each visit. If there are concerns about sedation at a particular dose, the MMT physician should schedule an assessment of the patient 2 to 6 hours after the methadone dose.

Take-Home Doses During Initial Titration

Generally**,** no take-home doses should be granted during the first 3 months of treatment including weekend take-home doses, holiday take-home doses, or pharmacy closures. Accelerated take-home doses after 2 months treatment may be considered under extraordinary circumstances (See Section 7.3.4 Accelerated

Take-Home Schedule). In the case of pharmacy closure with no reasonable alternative access to witnessed 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 7.3.2 Weekend Take-Home Doses when Weekend Pharmacy Access is Limited).

Sedating Drugs

Avoid initiating prescriptions for sedating drugs during the induction period and warn the patient to avoid using them without prior discussion with the MMT physician. Initiate these medications very cautiously during the stabilization phase. This includes benzodiazepines, non-benzodiazepine hypnotics, antipsychotics, antidepressants, dimenhydrinate (Gravol) and other sedating antihistamines. Even moderate, therapeutic doses of these 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.

Benzodiazepine Users

Benzodiazepine abuse and dependence are common in opioid-dependent individuals. 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 when attempted with methadone initiation. If possible, patients addicted to high doses (50 mg of diazepam equivalent per day) should be tapered to a lower dose prior to methadone initiation. Patients using lower doses should be monitored closely during induction. If benzodiazepine tapering during induction is considered, it should be carried out in a medically supervised setting. Only small benzodiazepine doses should be used – just enough to prevent severe withdrawal. Once stabilization on methadone is achieved, a tapering schedule should be started. Consultation with an addiction medicine physician is advised.

Baseline ECG

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 QTc interval (See Table 09: Risk Factors for QTc Prolongation in Patients on Methadone and Appendix H: Medications that Cause Prolonged QTc Interval). Patients with known risk factors for Torsades should have an ECG upon initiation of methadone.

Communication with the Pharmacist

Written treatment agreements and regular verbal communication about the patient's clinical presentation to both providers and pharmacists may enhance patient safety (See Appendix B: Sample Physician Pharmacist Treatment Agreement Letter).

Intoxication or Sedation at the Pharmacy

At any stage of MMT, the pharmacist should be instructed not to dispense the methadone and alert the physician if the patient appears sedated or intoxicated.

5.3 Clinical Criteria for Dose Adjustment

The physician should consider increasing the dose if the patient has cravings and opioid withdrawal symptoms, and/or ongoing opioid use (See Appendix K: Sample Methadone Maintenance Clinical Note). Withdrawal symptoms vary between patients.

Opioid withdrawal peaks at 2 to 3 days after the last use. Physical symptoms largely resolve by 5 to 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.

TABLE 03: OPIOID WITHDRAWAL SIGNS AND SYMPTOMS

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

A patient on an inadequate dose 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:

1. Gives an inconsistent history of withdrawal symptoms
2. Has one isolated symptom (such as insomnia or nausea)
3. Advises the onset of symptoms is not related to the time of the dose
4. 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.

5.3.1 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 symptoms include:

1. Medication use that speeds methadone metabolism (such as phenytoin, chronic alcohol use)
2. Opioid use
3. 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, day-time napping and other causes of night-time 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 counselling has failed. Trazodone or other non-benzodiazepine hypnotics are the treatments of choice.

Sedation and withdrawal symptoms are occasionally reported by patients 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 that is 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.

5.3.2 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 (i.e., what time of day they appear)
3. Ongoing drug use and timing of drug use:
   a. Opioid use at the end of the day may indicate inadequate methadone dose
   b. 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 methadone dose on the patient's underlying risk for methadone toxicity. See below table (Table 04: Patient Factors that Increase Risk of Methadone Toxicity[67-68]) for factors that increase this risk.

TABLE 04: PATIENT FACTORS THAT INCREASE RISK OF METHADONE TOXICITY[67-68]

High-Risk Patients
Recent benzodiazepine use
Use of other sedating drugs
Alcohol-dependent patients and heavy alcohol consumers (binge drinkers)
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

Opioid tolerance is difficult to establish by history; so, if in doubt, it is safer to initiate on a lower dose. Lowered tolerance is more 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 from opioids for more than 6 days (e.g., patients who have been recently discharged from a correctional facility, withdrawal management centre, or treatment centre).

TABLE 05: INITIAL METHADONE DOSE

Patient Factors	Initial Dose
No risk factors or recent abstinence	30 mg or less
Higher risk for methadone toxicity	20 mg or less
Abstinence from opioids for 7 or more days	10 mg or less

5.5 Induction Phase

The overall goal of the induction phase is to initiate on MMT.

5.5.1 Dosing During Induction Phase

Most patients in the induction phase are experiencing only partial relief of withdrawal symptoms, and they often continue to use opioids sporadically.

Dose increases during the induction phase should take place only after an in-person MMT physician or delegate assessment and for patients who are experiencing cravings, ongoing opioid use, and/or a cluster of opioid withdrawal symptoms (See Table 06: Dosing During Induction Phase).

MMT physicians should assess patients at least once weekly during this phase. Delegated providers may assess patients for dose increases as prescribed by a MMT physician if the physician is not able to see the patient with each dose increase.

Generally, MMT physicians should wait 5 days for a dose adjustment due to the long half-life and the subsequent time it takes for a change in dose to have its full effect. At induction, however, the physician is trying to balance dose changes that are frequent enough to keep patients in treatment, but at intervals long enough to be safe (i.e., reduce the risk of drug accumulation). As a result a 3-day interval has been largely accepted as reasonable up to 60 mg (a dose which almost all patients require). At 60 mg and above, the pace of dose increases needs to slow-down because the risk of drug accumulation becomes a greater concern than withdrawal symptoms affecting treatment retention. After reaching a dose of 60 mg a day, the frequency of dose increases should be changed to no more frequently than every 5 days (but every 7 days is recommended).

TABLE 06: DOSING DURING INDUCTION PHASE

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

5.5.2 Missed Doses During Induction Phase

Before proceeding to the next dose level during the induction phase, patients must have both:

1. At least 3 total days at the current dose AND
2. At least 2 consecutive days at the current dose on the days immediately preceding the dose increase

If 2 consecutive days are missed after consuming 1 or 2 days at a given dose level, the dose should be dropped to the previous dose level for at least 2 days.

If 2 consecutive days at any given dose are missed after having consumed that dose for 3 or more consecutive days, the same dose should be continued for at least 2 days prior to the dose being increased to the next dose level.

If 3 consecutive doses are missed at any time during the induction phase, the pharmacist should cancel the prescription until the physician can reassess the patient. The patient must be reassessed in-person by the physician and restarted at 30 mg or less for 3 days.

Collaborative communication between the physician and pharmacist is essential if the patient misses any doses during induction. The pharmacists should be advised to contact the MMT physician if the patient misses any doses.

See Section 5.7.1 Missed Doses During Maintenance Phase and Table 10: Management of Missed Doses for more information on managing missed doses.

The following chart illustrates appropriate management of missed doses during induction on MMT based upon the patient's recent history of consumed doses.

TABLE 07: MISSED DOSES DURING INDUCTION PHASE

Number of Missed doses during induction	Recommended daily induction dosage sequence (examples start with the third consecutive daily dose of 30mg)									
1 day missed	30 mg	40 mg	Missed dose	40 mg	40 mg	50 mg	50 mg	50 mg	60 mg	60 mg
	30 mg	40 mg	40 mg	Missed dose	40 mg	40 mg	50 mg	50 mg	50 mg	60 mg
	30 mg	40 mg	40 mg	40 mg	Missed dose	40 mg	40 mg	50 mg	50 mg	50 mg
2 days missed	30 mg	40 mg	Missed dose	Missed dose	30 mg	30 mg	40 mg	40 mg	40 mg	50 mg
	30 mg	40 mg	40 mg	Missed dose	Missed dose	30 mg	30 mg	40 mg	40 mg	40 mg
	30 mg	40 mg	40 mg	40 mg	Missed dose	Missed dose	40 mg	40 mg	50 mg	50 mg
3 days missed (requires physician assessment)	30 mg	40 mg	40 mg	40 mg	Missed dose	Missed dose	Missed dose	30 mg	30 mg	30 mg

5.6 Stabilization Phase

Dose increases during the stabilization phase should be preceded by an in-person MMT physician assessment and should only be given if the patient is experiencing cravings, ongoing opioid use, and/or a cluster of opioid withdrawal symptoms (See Section 5.3 Clinical Criteria for Dose Adjustment). The MMT physician should assess the patient prior to each dose increase during this phase.

5.6.1 Dosing During Stabilization Phase

TABLE 08: DOSING DURING STABILIZATION PHASE

Patient Factors	Dose Increase	Frequency
Higher risk for methadone toxicity	5-10 mg	Every 5 to 7 days
No risk factors or recent abstinence	10 mg	Every 5 to 7 days
Dose over 100 mg	10 mg	Every 7 to 14 days

5.6.2 Missed Doses During Stabilization Phase

If 3 or more consecutive doses are missed during the stabilization phase, the prescription should be cancelled. The patient must be reassessed by the MMT physician to obtain a new methadone prescription.

With respect to subsequent dosing, if 3 to 5 doses have been missed, the dose should be restarted at 50% of the last dose or at 50 mg, whichever is higher. The dose can then be increased by 10-15 mg every 1 to 3 days until the patient's original maximum dose is reached. If 6 to 10 days have been missed, the dose should be reduced to 30 mg, and can be increased by no more than 10 mg every 2 days until 60 mg a day, and then by 10-15 mg every 3 to 5 days until the patient's original dose is reached. If 11 or more doses have been missed, the patient should restart methadone according to the induction schedule (See Section 5.7.1 Missed Doses During Maintenance Phase and Table 10: Management of Missed Doses).

Dose increases during rapid re-stabilization can be supervised by a regulated healthcare provider formally delegated under Delegated Medical Function (DMF) providing the patients is seen by the MMT physician at least once a week.

5.7 Maintenance Phase: 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 to 8 weeks of initiating MMT. The optimal dose range for most MMT patients is 60-120 mg.[69-71] A 2009 meta-analysis reported that doses of methadone between 60-120 mg and individualization of doses are associated with better retention in MMT.[69]

Dose increases during the maintenance phase, are usually infrequent. If dose increases are required during the maintenance phase they should take place with an in-person MMT physician assessment and only for patients who are experiencing cravings, a cluster of opioid withdrawal symptoms, and/or ongoing opioid use. MMT physicians should assess patients when ongoing dose adjustments are occurring.

5.7.1 Missed Doses During Maintenance Phase

Standards for missed doses during maintenance are the same as those for the stabilization phase (See Section 5.7.1 Missed Doses During Maintenance Phase and Table 10: Management of Missed Doses).

5.7.2 Doses Below 60 mg

There is evidence that methadone doses of 60–120 mg are more effective in reducing heroin use and retaining patients in treatment than doses below 60 mg.[69-73] However, maintenance doses below 60 mg may be justified, based on the clinical situation 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

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 QTc interval, which can cause Torsades, a ventricular arrhythmia.[51] 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.[58] 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 QTc syndrome, liver dysfunction, electrolyte disturbances, and medications that affect methadone levels or the QTc interval (See Appendix H: Medications that Cause Prolonged QTc Interval).[51-55]

While it seems to be dose-dependent, it is important to note that sudden cardiac death associated with methadone has been seen at dosages as low as 29 mg a day.

This means that arrhythmia can occur in dosages commonly used to treat addiction, and that dosage is just one consideration with regard to limiting arrhythmia risk.[56]

5.7.3.2 Assessment and Monitoring

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, the pharmacist or the patient's family has observed cognitive effects such as "nodding off," lethargy, or diminished concentration or memory.

In addition to a baseline ECG at induction for patients with risk factors for Torsades de Pointes, an ECG should be done on patients whose dose is 150 mg or greater[74-75] and then repeated after every 30-50 mg increase in dose.

TABLE 09: RISK FACTORS FOR QTC PROLONGATION IN PATIENTS ON METHADONE[IV]

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	See Appendix A: Drug to Drug Interactions
Alcohol use	
Cocaine use	

IV Table is adapted from: *Methadone – associated QTc prolongation: A case report and review of the literature* (See *Appendix G: Behavioural Addictions*).[51]

Family or past history of long QTc syndrome	History of syncope or sudden cardiac death in the family
On medications that prolong QTc	See Appendix H: Medications that Cause Prolonged QTc Interval

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 QTc interval is elevated (Women <460ms and Men<440ms). 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 and consider alternatives such as buprenorphine.

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 of ongoing withdrawal symptoms 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 that induce the CYP 450 3A4 enzyme system such as phenytoin and chronic alcohol use, may decrease a patient's methadone levels (See Appendix A: Drug to Drug Interactions).

Continued Opioid Use
Continued opioid use causes increased tolerance and withdrawal symptoms with opioid cessation.

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

Pseudo-Normalization
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 metabolism 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.

Pregnancy
See Section 12. MMT Considerations During Pregnancy.

5.8 Summary of 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. The reasons for the missed doses should always be discussed with the patient and documented in the clinical records. 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 3 consecutive days.

During the maintenance phase, if a patient has missed methadone doses for 10 days or less, the MMT physician may restabilize the patient up to their previous maintenance dose at a rate more rapid than 10 mg every 5 days (See Standard 13, Section 5: Dosing During Induction, Stabilization and Maintenance). Until the previous maintenance dose is reached, in-person assessment by the MMT physician for each dosage increase (as written on a duplicate prescription) is not necessary, provided that the dose increase is being supervised by a delegated provider in communication with the MMT physician. If the MMT physician's written instructions for a planned dose increase cannot be implemented for any reason, the MMT prescriber should be contacted.

TABLE 10: MANAGEMENT OF MISSED DOSES

Phase of Treatment	Missed Doses	Action	Action / Dose Change
Induction	1 day missed	No dose increase	Resume same dose Before proceeding to the next dose level patients must have both: At least 3 consecutive days at the current dose At least 2 consecutive days at the current dose immediately before the dose increase
Induction	2 consecutive days missed	Dosage adjustment	If 2 consecutive days are missed after 1 or 2 days at a given dose level, the dose should dropped to the previous dose level for at least 2 days. If 2 consecutive days at a given dose are missed after having been on that dose for 3 or more consecutive days, the same dose should be continued for at least 2 days prior to the dose being increased to the next dose level.
Induction	3 or more consecutive days	Cancel remainder of prescription Reassess patient in person	Restart at initial dose (10-30 mg) for at least 3 consecutive days Reassess after 3rd consecutive dose
Stabilization/ Maintenance	1 to 2 days missed	Provide usual prescribed dose if patient is not intoxicated Assess patient in 1 to 2 weeks to determine clinical stability	No change
Stabilization/ Maintenance	3 to 5 consecutive days missed	Reassess patient in person Cancel remainder of prescription	Restarted at 50% of regular dose or decrease to 50 mg (whichever is higher) The dose can then be increased by no more than 10-15 mg every 1 to 3 days until the patient's original maximum dose is reached

Phase of Treatment	Missed Doses	Action	Action / Dose Change
Stabilization/ Maintenance	6 to 10 consecutive days missed	Reassess patient in person Cancel remainder of prescription	Restart at 30 mg or less then increase by no more than 10-15 mg every 2 days until 60 mg per day, then by 10-15 mg every 3 to 5 days until patient's original dose is reached
Stabilization/ Maintenance	11 or more consecutive days missed	Reassess patient in person Cancel remainder of prescription	Same as a new induction

5.9 Split Doses

Split dosing is occasionally used during the management of pregnancy, chronic pain, or in patients on medications that induce rapid metabolism of methadone (See Section 10.1.5.1 Methadone for Analgesia and Section 12.2.2.2 Dose Adjustments During Pregnancy).

5.10 Vomited Doses

When a patient reports that they have vomited their dose, that dose should not automatically be replaced.

Best practice recommends not replacing the dose unless the vomiting was witnessed by a health professional on the MMT team. The patient should contact the physician (or the pharmacist may do so if they have witnessed the incident) and provide him or her with as much information as possible about the incident (time the dose was taken, time of vomiting, etc.).

Physicians can authorize replacement doses by sending a written authorization to the pharmacy (requires a new NSPMP duplicate prescription). This authorization stays with the original prescription for the duration of the dispensing and storage requirements. Because it is difficult to completely empty the stomach by emesis, it's important to note that the repeated dose replacement can lead to overdose.

Should it be agreed that a prescription for a replacement dose be issued, the following guideline is offered:

- Emesis < 15 minutes after consumption – replace 50% to 75% of the full dose
- Emesis between 15 - 30 minutes after consumption – replace 25% to 50% of the dose
- Emesis > 30 minutes after consumption – no replacement

The underlying causes of vomiting should be addressed. In 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 clinic staff did not observe emesis (See Section 12.2.2.3 Managing Vomited Doses).

5.10.1 Vomiting in Pregnancy

The risks associated with vomited doses are higher in pregnant patients than in other patients. For this reason, replacing vomited doses should be considered even if not witnessed. Consideration should be given to replacement doses on the higher end of the dose range recommended above. If emesis is a problem during pregnancy, the patient should stay in the pharmacy after dosing to be observed for vomiting (for 15 to 30 minutes).

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.

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.[76-77] Providing take-home doses to methadone patients with drug-free UDS is an effective strategy for reducing opioid and other drug use (contingency management).[78-82, 24]

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).

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, using strategies such as witnessed collection or supervised collection, including temperature monitoring, measurement of pH, creatinine, or specific gravity.
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 L: Urine Drug Test Interpretation).
5. The 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.

6.1 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).

6.2 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 11: Methods of Tampering and Monitoring Process.

TABLE 11: 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

6.2.1 Method of Collection

Urine for drug screens should be collected in the office (either witness 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-labelled 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 clinic staff member.

6.3 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 L: 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 counselling 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.

6.4 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 as well as NSPMP patient profile.
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.

6.5 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.

6.5.1 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, 4 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 2 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 7.6 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 obligations.

7. Take-Home Doses

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

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.[83-87, 24]

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).[88-92, 24] 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.[93-95]

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 should not prescribe take-home doses before 3 months in the MMT program (See Standards 9, 10 and 11, of Section 7. Take-Home Doses for unique exceptions).
3. The MMT physician should prescribe a maximum of 6 take-home doses per week.
4. On the day the MMT patient picks up their take-home doses, the ingestion of dose for that day must be witnessed.
5. The MMT patient shall return all take-home dose bottles to the pharmacy before receiving the next take-home doses.
6. 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, non-prescribed opioids, or benzodiazepines)
   c. The patient is not able to safely store the methadone
   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
7. 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 3 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.

8. The daily observed dose should 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.
9. 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 in Standard 6, Section 7. Take-Home Doses is present
10. 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 in Standards 6, Section 7. Take-Home Doses is present
11. 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 in Standards 6, Section 7. Take-Home Doses is present
12. 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 7.5.2 Suspending Take-Home Doses for Reasons Other than Substance Use).
13. The MMT physician should suspend take-home doses for patients who consume them early, or who report lost or stolen take-home doses even on one occasion.
14. Patients wishing to receive take-home doses should have random weekly UDS that are negative for 4 consecutive weeks prior to obtaining take-home doses. After take-home doses have been initiated, random UDS should be obtained weekly for a minimum of 4 weeks and then every 2 weeks for a minimum of 8 weeks. The frequency of random UDS may then decrease to once monthly according to individual clinical and social circumstances.
15. 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.
16. 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 Guidelines 14 and 15 of 7. Take-Home Doses and Section 7.6 Take-Home Doses for Patients on Benzodiazepines or Opioids).
17. 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 should be reassessed.

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. Having the patient complete a written take-home dose agreement is highly recommended.
3. The MMT physician should ensure the first take-home dose is prescribed only after 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 1 take-home dose per week increasing at a rate of no more than 1 take-home dose per week every 4 weeks, to a maximum of 6 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.

b. **Schedule B**: Starting with 2 daily take-home doses on consecutive weekend days. After a further 8 weeks free of substance use, take-home doses are increased to 1 carry of 3 consecutive days and 1 carry of 2 consecutive days with intervening witnessed doses. After an additional 12 weeks free of substance use take-home doses can be increased to 6 take-home doses a week.

4. In the accelerated schedule, 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 1 extra take-home dose per week, every 2 to 4 weeks, to a maximum of 6 take-home doses per week.
5. 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.
6. MMT physicians working in communities without a pharmacy open 7 days per week should consider negotiating with the local hospital to provide weekend dispensing, or arranging for the methadone to be dispensed at the nearest hospital.
7. The MMT physician may give 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 6 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 2 months and have had at least 4 weeks of negative UDS, and are approaching a stable methadone dose, and are receiving 1 to 2 take-home doses per week. A maximum of 6 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.
8. If a local pharmacy cannot be found, 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.
9. During a relapse for any drug use, the MMT physician should immediately suspend all take-home doses until restabilization has been demonstrated via negative UDS for at least 1 month, and then reinstate at a rate of 1 take-home dose per week to 1 take-home dose per month depending on the reliability of the patient and demonstrated abstinence.
10. During a relapse of greater than 1 month, the MMT physician should suspend all take-home doses until restabilization has been demonstrated via negative UDS for at least 2 months. Take-home doses may then be reinstated at the regular rate using 1 of the protocols in Guideline 3, Section 7. Take-Home Doses contingent on negative UDS and no reported drug use.
11. 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
12. 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 1-month period at a rate of 1 take-home dose per week to 1 take-home dose per month depending on the patient's

reliability and clinical stability.

13. 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.
14. 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 7.6 Take-Home Doses for Patients on Benzodiazepines or Opioids.
15. The MMT physician should not prescribe take-home doses to patients who refuse consent to communicate with their opioid or benzodiazepine prescriber.
16. Patients may be given 13 days of take-home doses, if specific criteria are met (See Section 7.7 Routine 13-Day Take-Home Doses for Work Commitments).

7.1 Take-Home Doses: Risks

7.1.1 Diversion

To reduce the risk of diversion and the associated societal harms, the MMT patient must have witnessed ingestion of the methadone dose on the day they pick up their take-home doses.

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.[96]

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.

7.1.2 Locked Box

To increase the safety of storing methadone at home, patients can be asked to use locked boxes.[97]

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. The *Methadone Maintenance Treatment Services: Standards of Practice for Community Pharmacies in Nova Scotia* (NSCP) 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.

7.2 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 (NSCP).

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 4 weeks and then every 2 weeks for a minimum of 8 weeks. The frequency of UDS may then decrease to once a month depending on the clinical situation.

A written take-home dose agreement is highly recommended (See Appendix M: Take-Home Dose Agreement).

7.3 Take-Home Dose Acquisition Schedules

7.3.1 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.

7.3.2 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.

7.3.3 Subsequent Take-Home Dose Acquisition

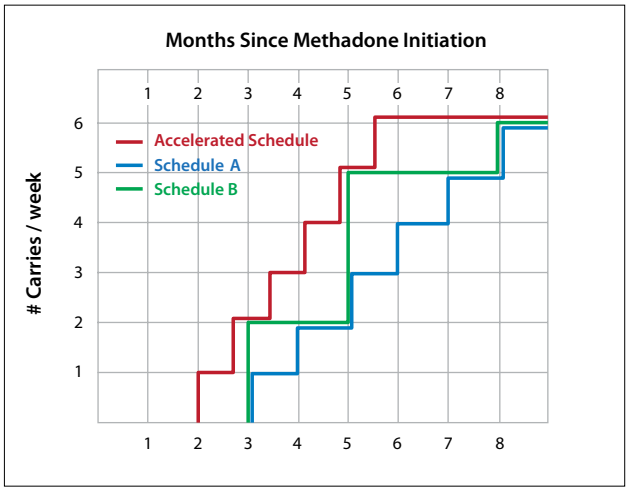
Subsequent increases in take-home doses occur no more often than every 4 weeks with evidence of clinical stability according to **one** of the following schedules:

Schedule A: Starting with 1 take-home dose/week increasing at a rate of no more than 1 take-home dose per week every 4 weeks, to a maximum of 6 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 2 daily take-home doses on consecutive weekend days. After a further 8 weeks free of substance use take-home doses are increased to one carry of 3 consecutive days and one carry of 2 consecutive days with intervening witnessed doses. After an additional 12 weeks free of substance use take-home doses can be increased to 6 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



7.3.4 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 2 months, with 1 additional weekly dose every 2 to 4 weeks. Patients should have at least 4 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.

7.4 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) 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 12: 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 12: CRITERIA FOR PRESCRIBING EXCEPTIONAL TAKE-HOME DOSES

IF:	THEN:
The patient has been on MMT for at least 2 months and is not yet eligible for any take-home doses, but is stable and is not considered high-risk for diversion.	1. Give take-home doses on compassionate grounds only (e.g., a personal crisis) 2. Give no more than 6 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.	1. Give take-home doses for sound personal reasons only (e.g., vacation/holidays, family matters) 2. Give no more than 6 take-home doses
The patient has not had drug use for 12 months, is clinically stable and receiving 3 to 6 take-home doses per week.	1. Give up to a 13-day take-home dose for travel purposes 2. If more than 13 days of take-home doses is required, a second opinion with another MMT physician is suggested

7.5 Suspending Take-Home Doses

7.5.1 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 at 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 counselling 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 counselling and follow-up should be increased, and take-home doses should be reinstated at a gradual rate when the relapse has resolved.

7.5.2 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.

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 Guidelines 3, 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.

7.6 Take-Home Doses for Patients on Benzodiazepines or Opioids

Take-home doses may be considered for clinically stable patients who are prescribed benzodiazepines or opioids only in specific circumstances. Long-term benzodiazepine use is generally inappropriate, and patients should not be eligible for take-home dose while on benzodiazepines or opioids unless there are exceptional circumstances. Take-home doses may be allowed to continue under exceptional circumstances where opioids are prescribed or recommended for acute pain, or prescribed or recommended by a pain specialist for chronic pain, or benzodiazepines are prescribed or recommended by a treating psychiatrist or neurologist.

Where benzodiazepines or opioids are being prescribed, dispensing by the same schedule as the methadone is strongly recommended.

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 if the patient:

a. Has a medical or psychiatric diagnosis that is currently stable and warrants the use of the benzodiazepine or opioid
b. Is on a low to moderate therapeutic dose of the benzodiazepine or opioid
c. Has not shown signs of benzodiazepine or opioid misuse or toxicity
d. Provides consent for the MMT physician to discuss their management with their opioid or benzodiazepine prescriber
e. Is prescribed and dispensed the medications with controlled dispensing, usually in a similar fashion to their methadone dispensing
f. Meets all other criteria for take-home dose eligibility

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 10.3.2 Sedative-Hypnotics Including Benzodiazepines.

MMT physicians should not prescribe take-home doses for patients who refuse consent to contact the opioid or benzodiazepine prescriber.

The MMT physician may also taper the methadone if there is a strong possibility that the patient is misusing the medications or is on an unsafe combination. The MMT physician may contact the other non-MMT prescriber without the patient's consent if there is an imminent risk of harm.

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

In exceptional circumstances, some patients who are on 6 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 social supports and is engaging in counselling.[98]

Overview

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 social supports and is engaging in counselling.[98] Ideally the period of abstinence from illicit substances should be at least 1 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 2 or more years will have better outcomes when tapered off methadone than those who start the tapering process before 2 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.

Voluntary Withdrawal

STANDARDS

None for this section.

GUIDELINES

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

Involuntary Withdrawal

STANDARDS

1. Once involuntary tapering has begun, all methadone doses must be daily witnessed ingestion.

GUIDELINES

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 transfer the patient to 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 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.
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 counselling and support.

8.1 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 N: Sample Tapering Readiness Questionnaire). In one study, 46% of subjects remained abstinent after an average of 2.4 years post-MMT.[100] 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%.[101] Success rates are higher for patients who have been on MMT for 2 years or more.[102-104]

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.[105] 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 1-2 mg every 1 to 4 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 counselling are very important at this stage.

Patients should not be penalized for unsuccessful weaning from MMT.

8.2 Involuntary Withdrawal

8.2.1 Indications for Involuntary Withdrawal

The decision to involuntarily withdraw a patient 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 withdraw include:

- Threats to staff members or others
- Disruptive behaviour at the 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.

8.2.2 Process for Involuntarily Withdrawing a Patient

Recommendations to effectively end the doctor-patient relationship 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 CPSNS 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 n MMT physician-patient relationship, download CPSNS: *Ending the Physician-Patient Relationship*.

Download CPSNS Guidelines PDF here
Visit website: www.cpsns.ns.ca/PhysicianGuidelinesandPolicies.aspx?EntryId=14

MMT patients who feel that they have been wrongfully dismissed can contact CPSNS 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. Counselling and Case Management

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

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 spiritual approach to help patients cope with their problems. When counselling 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 counselling 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.

STANDARDS

1. The MMT physician shall provide counselling to willing patients or refer them to counselling 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.

GUIDELINES

None for this section.

9.1 Treatment Team

Collaborative practice in MMT is considered best practice. Ideally, the MMT patient should have access to a team that includes physicians, nurses, social workers, addiction services, therapists, psychologists, case managers, peer support workers, and pharmacists. 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.

9.2 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. These treatment goals should be chosen by the patient, not the physician. Many appropriate treatment goals are not necessarily focused on drug-using behaviour. For example, patients may wish to move to better or safer housing, improve their general health, enrol 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 counsellors (See Appendix C: Resources), or may refer patients to independent counselling 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 counsellors. 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.

9.3 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."[106] 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 Nova Scotia 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. District Health Authorities should provide such support to MMT prescribers practicing within the district.

Case management should be offered regardless of where the individual is in the system.[107]

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

9.4 Therapeutic Factors

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

9.4.1 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.[108-109, 105] 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 counselling, it is essential to connect the patient with services in the community.

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

9.4.2 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.[105] Providing counselling 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 counselling and help. These services are offered by addiction services personnel employed by the Nova Scotia Department of Health and Wellness at various locations throughout the province (See Appendix C: Resources). MMT physicians in those communities 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 counselling
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 counselling
3. Help with referrals to community resources
4. Filling out forms and applications, providing letters

9.4.3 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.

> **Download** Guidelines PDF here
> **Visit website**: www.knowledgex.camh.net/amhspecialists/promotion/Pages/recovery.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 CPSNS Policy for Medical Record Keeping.

> **Download** CPSNS Policy for Medical Record Keeping here
> **Visit website**: www.cpsns.ns.ca/PhysicianGuidelinesandPolicies.aspx?EntryId=5

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.

9.4.4 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.

9.4.5 Counselling Techniques and Skills

There is evidence of the impact of counselling. Recent studies recommend that MMT physicians be willing and able to provide counselling to their MMT patients.[110] In a recent survey of MMT patients in Ontario,[105] 27% indicated they received counselling from MMT physicians (either alone or in addition to other support), 18% received counselling from a nurse and 12% received counselling from a psychiatrist (either alone or in addition to services from another agency).

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

MI is a counselling 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 counsellor. It has been shown to be particularly helpful in working with people who use substances.[111] 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, the family can be a valuable resource for the patient and their 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. It is important to note that families affected by other's addictions will also need support and this is offered through Addiction Services.

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 instil 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

9.5 Community Resources

Addiction Services is operated by the District Health Authority in your community.

Visit website: www.addictionservices.ns.ca

To find the Addiction Services office closest to you, click on the region of the map where you live. If you are looking for the provincial Department of Health Promotion and Protection, visit: www.gov.ns.ca/hpp/addictions (See Appendix C: Resources).

10. MMT with Concurrent Mental and Physical Disorders

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

Overview

MMT physicians must 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 preferably have an identified primary care physician. The MMT physician, if not the patient's family physician, should encourage the patient to see their primary care physician regularly for ongoing preventive care, screening, and chronic disease management.

Chronic diseases commonly associated with the MMT patient population for addiction include chronic pain, diseases caused by blood-borne pathogens such as Hepatitis B and C, HIV, and a variety of mental illnesses. Concomitant substance use disorders will also be dealt with in this section.

Those physicians requiring an exemption to prescribe methadone for opioid dependence have an interest and expertise in the treatment of addiction (See Section 2.1 Obtaining a Methadone Exemption). MMT physicians cannot prescribe methadone as an analgesic for non-addicted patients with chronic pain, unless they have the specific exemption for analgesia from Health Canada. This exemption is independent of the exemption for methadone as a treatment of addiction.

MMT physicians with the Health Canada exemption for opioid dependence can prescribe methadone both as an analgesic and as an opioid substitution therapy for patients who have concurrent addiction and acute pain. However, for chronic pain management – where, over time, the treatment of pain (rather than that of opioid dependence) becomes the primary focus of the patient's care – the MMT physician requires an exemption to prescribe methadone for pain.

STANDARDS

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

GUIDELINES

2. The MMT physician should encourage patients to attend a primary care physician or team for ongoing, age-appropriate screening and chronic disease management if it is not feasible for the MMT prescriber to provide this care.
3. The MMT physician should have open and regular communication with the patient's primary-care physician.
4. MMT physicians should screen patients for Hepatitis C and HIV, and offer referral and treatment when clinically indicated.
5. MMT physician should screen for Hepatitis A and B when appropriate, and arrange immunization.
6. The MMT physician should assess the patient periodically for alcohol use through an alcohol consumption history (screening questionnaires and laboratory measures might also be considered).

7. For patients with acute pain that warrants short-term opioid therapy, MMT physicians may prescribe opioids in addition to methadone or may temporarily split the methadone dose with an additional 10-15 mg evening dose.
8. If opioids are prescribed for acute pain, the MMT physician should choose an opioid that the patient has not misused in the past, and consider prescribing a sustained release opioid formulation (e.g., morphine SR TID) dispensed at a frequency consistent with methadone dispensing.
9. The MMT physician should become familiar with the Canadian Guideline for Safe and Effective Opioid Use in Chronic Non-Cancer Pain (http://nationalpaincentre.mcmaster.ca/opioid).
10. The MMT physician should only attempt long-term opioid therapy for methadone patients with chronic non-cancer pain in formal or informal consultation with a pain consultant.
11. 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 eligible for take-home doses or receiving take-home doses.
12. The MMT physician should only attempt long term opioid therapy if the patient has had insufficient analgesic benefit from an adequate trial of non-opioid treatments and from a trial of split methadone dosing.
13. 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.
14. 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

10.1 Physical Disorders

10.1.1 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.[112-113] Patients with HIV should be referred to infectious diseases or an HIV clinic.

When Hepatitis C is present, physicians should focus on the following areas:

Lifestyle

- Advise patients against alcohol consumption
- Discuss appropriate diet
- Discuss risk of transmission

Immunization

Vaccinate patients against Hepatitis A and B, and provide other relevant vaccinations

Treatment

Refer to a physician with expertise in Hepatitis treatment when indicated

Physicians should attend to the following issues with HIV-positive patients:

Education

Educate patients on taking precautions with sexual relationships and shared needles

Immunization

- Arrange for patients to be vaccinated against Hepatitis A and B
- Immunize patients with tetanus toxoid, pneumococcal vaccine and influenza vaccine

Testing and Monitoring

- Consider tests for tuberculosis and syphilis
- Monitor patients' CD4 T- cell counts and viral loads

Treatment and Referral

- Refer to an infectious disease specialist for assessment and treatment
- Be aware of the many drug interactions between methadone and HIV medications, and make dose adjustments as clinically indicated

10.1.2 Hepatitis A and B

MMT patients should be tested for their immunity to Hepatitis A and B, and if not immune, immunized appropriately. Patients with Hepatitis B or C should be referred to the liver clinic or to infectious diseases clinic.

10.1.3 Hepatic, Renal, Respiratory and Cardiac Disease

Hepatic Disease

While stable liver dysfunction does not appear to affect methadone levels,[114-115] MMT patients with decompensated cirrhosis may become very sedated. The MMT physician should consider decreasing the dose in this circumstance, and benzodiazepines must be avoided. The half-life of benzodiazepines can be prolonged in hepatic dysfunction, and benzodiazepines can trigger encephalopathy. The QTc interval should be monitored, as liver dysfunction is a risk factor for Torsades de Pointes arrhythmias.[52]

Renal Disease

Evidence suggests that the metabolism of methadone is not affected by renal insufficiency.[116, 117] 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., asthma, pneumonia, COPD exacerbation) should be closely monitored for both worsening respiratory function and methadone toxicity.

Cardiac Disease

Patients who have cardiac disease are often at higher risk for arrhythmias, therefore their QTc interval should be closely monitored. Before initiation on MMT, careful evaluation of cardiac symptoms (syncope, palpitations) and detailed cardiac personal and family history should be obtained. Obtain a baseline and periodic ECG as indicated. Consideration should be given to a cardiology referral if there are any concerning features on history or physical exam.

10.1.4 Acute Pain

MMT patients are tolerant to the analgesic effects of opioids.[118] Severe acute pain (i.e., renal colic, severe trauma, post-op pain, etc.) may require opioids in higher and/or more frequent doses than in less tolerant patients

In MMT patients who have severe pain unresponsive to non-opioid treatments, 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.

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, the use of morphine is preferred over oxycodone or hydromorphone.

SR morphine or Kadian should be considered as it avoids peaks and troughs and sustains analgesia over night. An alternative option to opioid therapy that may be helpful is temporarily adding an afternoon or evening methadone daily dose (e.g., 10-15 mg) for patients who have take-home doses. Formal or informal consultation with a more experienced MMT prescriber should be considered at any point as required.

10.1.5 Chronic Non-Cancer Pain

Chronic non-cancer pain is common in MMT patients.[119] 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.

> **Download** CPSNS Guidelines PDF Part A and Part B
> **Visit website**: www.cpsns.ns.ca/PhysicianGuidelinesandPolicies.aspx?EntryId=14

MMT patients with CNCP present clinical challenges that require special consideration when prescribing opioids.

10.1.5.1 Methadone for Analgesia

Controlled trials have found that methadone is of comparable effectiveness to morphine as an analgesic.[120-121] The duration of analgesic action of methadone is typically no more than 8 hours.[122] Patients with concurrent pain and opioid addiction often experience pain relief once methadone treatment is initiated. When an optimal dose for withdrawal management is reached, and if all non-opioid therapies have failed, the methadone dose may be split for patients who are on take-home doses. Formal or informal consultation with a physician experienced in methadone and chronic pain management should be considered.

10.1.5.2 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.

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). Consultation with an experienced MMT prescriber is recommended before embarking on long-term opioid treatment for MMT patients

10.1.5.3 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.

The methadone monitoring program offered by Nova Scotia NSPMP is an especially important component of the care of patients who must be on both methadone and opioids. Although recommended for all MMT patients, it is critical in this situation to get a prescription monitoring report (patient profile from the NSPMP) on all patients during initiation, periodically, and at any sign of deterioration in stability.

When a patient requires a second opioid in addition to methadone, it is preferred that the MMT physician prescribes both the opioid and the methadone. If the MMT physician knows that another physician is prescribing opioids for the patient, several other 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 (See Section 5.2 Strategies to Reduce Risks of Methadone).

TABLE 13: OVERVIEW OF PAIN MANAGEMENT

Pain Condition	Management
Mild to moderate pain	Non-opioid treatments
Severe pain condition that usually requires opioid therapy	Formal or informal consultation with chronic pain management specialists **First-line**: Non-opioid treatments **Second-line**: Split methadone dose **Third-line**: Sustained release opioid (e.g., morphine)

10.2 Mental Illness

10.2.1 Anxiety and Mood Disorders

The prevalence of anxiety and mood disorders is several times higher in MMT patients than in the general population.[123-124] At least 30% of substance-dependent patients meet the Diagnostic and Statistical Manual of Mental Disorders' (DSM-IV-TR) criteria for an Axis I psychiatric disorder, unrelated to drug use or withdrawal. Depression, anxiety, bipolar disease and eating disorders are common, as are personality disorders such as antisocial personality disorder.

Identifying and providing treatment for mental health disorders can help improve methadone maintenance treatment outcomes, including reduced use of drugs and treatment retention.

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

10.2.2 Management Issues

The initial assessment should always include screening questions for comorbid mental illnesses. When assessing for mental illness independent of drug use, past psychiatric treatment, a family history of mental illness and drug-free periods are very important considerations. It may be difficult to determine whether a psychiatric disorder is the primary condition or whether it is secondary to drug use. For example, use of some substances such as alcohol may either cause symptoms, which present as mental illness (such as depression), or may interfere with the management of an underlying mental illness. The distinction may be easy to make if symptoms are rapidly resolved when the intoxication state subsides (as in the case of cocaine and its resulting psychosis). In general, however, to rule out substance-induced disorders, a skilled assessment is required

that should take into account how symptoms respond to increases or decreases in drug use, or periods of abstinence. Substance-dependent patients also have a significantly higher incidence of sexual abuse issues and eating disorders. In these cases, treatment and focused counselling to assist recovery may be beneficial. Mental Health Services should be consulted for further assessment and treatment. The Best Practices document from Health Canada for the treatment of Concurrent Mental Health and Substance Abuse Disorders further outlines guiding principles for the treatment of concurrent disorders.

> **Download** Best Practices PDF here
> **Visit website**: http://www.hc-sc.gc.ca/hc-ps/pubs/adp-apd/bp_disorder-mp_concomitants/index-eng.php

10.3 Poly-Substance Comorbidity

Methadone maintenance treatment is very successful at reducing the harm associated with opioid use, but ongoing use of other mood-altering drugs reduces that benefit.

As poly-substance use is very common among people who are dependent on opioids, practitioners delivering methadone maintenance treatment will almost certainly have to deal with this issue**.**

Consequently, methadone prescribers should pay attention to their patients' use of other mood-altering drugs – both prescription (benzodiazepines, for example) and non-prescription. All patients require a comprehensive assessment that includes a detailed inventory of all drugs used, leading to a diagnosis and treatment plan for each patient.

10.3.1 At-Risk Drinking

At-risk drinking and alcohol dependence are common among MMT patients.[125-126] Excessive alcohol use accelerates liver damage in patients with Hepatitis C.[127] 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.

Alcohol has the potential to interact with methadone in a harmful way. It is recommended that patients on MMT be encouraged to minimize alcohol consumption as much as possible. Abstaining completely from alcohol is recommended for patients with Hepatitis C.

Alcohol abuse in MMT patients should be aggressively addressed to reduce the risk of overdose.

Alcohol use also poses unique concerns in methadone maintenance patients. The risk of overdose increases with use of alcohol, given the synergistic respiratory depressant effect alcohol has with methadone. In addition, alcohol interferes with the metabolism of methadone. In its early stages, alcohol abuse has the potential to induce hepatic enzymes, which can accelerate methadone metabolism. At the very end stages, liver failure can precipitously reduce the methadone tolerance of a patient. For these reasons, methadone should be used with caution in end-stage liver disease. These complicated interactions underscore the need for physicians to appropriately screen and monitor their patients for alcohol use and aggressively address alcohol abuse-related issues when present.

Methadone treatment does not appear to significantly reduce alcohol consumption in the long-term.[58, 128-129] Evidence suggests that counselling about alcohol use is effective in methadone patients.[130]

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

Pharmacotherapy
Naltrexone (ReVia®) is contraindicated in patients on methadone. Available alternatives include disulfiram and acamprosate.

Alcohol Withdrawal
Methadone patients in alcohol withdrawal should be managed in a withdrawal management unit.

10.3.2 Sedative-Hypnotics Including Benzodiazepines

Comorbid sedative-hypnotic use poses another set of unique challenges. Like alcohol, these drugs have a synergistic respiratory depressant effect when used with methadone, and may increase the risk of fatal overdose. The issue of multi-doctoring, where patients may be receiving sedative-hypnotics from other physicians, may need to be addressed.

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.[131-132, 65, 133-136] Results regarding the impact of benzodiazepine use on treatment retention have reported either a negative impact[137] or no impact on treatment retention.[138] There is no beneficial impact of benzodiazepines on treatment retention. As well, an observational study documented reduced symptoms of depression in MMT patients who were tapered off benzodiazepines and started on antidepressant therapy.[139]

Sedative-hypnotics need to be used cautiously, if at all, in patients with addiction disorders. There is little evidence and few indications for long-term benzodiazepine use. As there is added risk with benzodiazepine use in MMT patients, all long-term benzodiazepine use should be gradually discontinued.

10.3.3 Stimulants

Patients may still meet the criteria for opioid dependence when it is apparent that stimulants, whether cocaine or methamphetamine, are the drugs of choice.

Failure to recognize stimulant abuse or dependence as a problem may undermine a methadone maintenance program.

A trial of methadone maintenance treatment may be appropriate, but a plan to deal with the stimulant use should be in place from the beginning. MMT should only be continued long-term if objective benefits can be documented. Furthermore, the treating physician should be prepared to review and update the treatment plan at each visit.

10.3.4 Marijuana

The ongoing use of mood-altering drugs such as marijuana can undermine the efforts being made in treatment to develop non-chemical coping strategies. While there is controversy as to whether or not marijuana causes an "amotivational syndrome," there is evidence that both anxiety and psychosis can be exacerbated by or result from marijuana use.

Perhaps most importantly for the MMT patient, the procurement of marijuana often keeps patients connected to their drug dealers, which can remain a significant trigger for relapse.

11. Methadone Toxicity

Methadone toxicity presents a serious challenge to MMT physicians. The most likely time for a patient to experience toxicity is during the induction phase.

Overview

Methadone toxicity presents a serious challenge to MMT physicians. The most likely time for a patient to experience toxicity is during the induction 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 that is tolerant to another opioid is still at risk for methadone toxicity. There can be considerable variation between patients in how methadone is metabolized.

Overdose leading to opioid toxicity is characterized by a decreased level of consciousness, respiratory depression, and pinpoint pupils.

Two features of methadone toxicity make interpretation of these signs difficult:

1. Definite signs of methadone toxicity may occur within 3 to 4 hours but may not become apparent for 5 to 9 hours after the overdose.[65, 140]
2. MMT patients who have had an overdose may appear relatively alert during conversation, succumbing to respiratory depression during sleep.[141]

STANDARDS

None for this section.

GUIDELINES

1. The MMT physician should assess patients in-person or refer them to the emergency department if they might have taken a dose above what would be considered a safe dose, given their underlying tolerance, concurrent medication use, and health status.
2. If, after assessment, 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 that an ambulance is being called
   b. Ensure a staff member keeps the patient awake until the ambulance arrives
   c. Arrange an involuntary mental health assessment if the patient refuses to attend the emergency department

11.1 Dosing and Assessment for Possible Methadone Toxicity

11.1.1 Definition of a Toxic Dose:

Reasonable dose increases are usually in the range of 10 mg every 3 days or 15 mg every 5 days. Intentional dose increases in excess of 15 mg are not considered safe and acceptable practice (See Section 5.4 The Initial Methadone Dose).

If a patient has consistently been on 50 mg per day for several weeks and then receives 60 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 40 mg on the second day, they could be at risk of methadone toxicity.

In the case of prescriber or pharmacy error, or if non-prescribed (diverted) methadone is ingested where 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, as well as the timing of dose increases. Even "extra" doses that are considered "small" for example 15-20 mg can cause toxicity during induction of methadone, or if the patient is elderly or has a respiratory illness. Because of the long half-life of methadone, increasing doses too frequently can lead to toxicity. At the time of methadone induction, it is important to discuss with the MMT patient the risks of overdose (See Section 5.2 Strategies to Reduce Risks of Methadone and Appendix J: Patient Guide on Methadone Overdose).

11.1.2 Assessment of the MMT Patient Who May Have Taken a Toxic Dose:

If the patient is currently at the clinic, the MMT physician or delegate should engage the patient in conversation for at least five minutes, as an overdosed patient will 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 arousable. Remember that the peak effect of the methadone is usually apparent 3 to 4 hours after ingestion,[64] but may take as long as 5 to 9 hours or more.

11.2 Patient Referral to the Emergency Department for Overdose

The management of methadone overdose is described in detail in Section 5.2 Strategies to Reduce Risks of Methadone. When a patient is sent for emergency treatment, the appropriate documentation should be completed, and given to the paramedics or faxed to the emergency department. If possible, the MMT physician should speak directly with the attending emergency department physician or nurse.

A patient in the Emergency Department with a suspected methadone overdose should be:

1. Observed for a minimum of 10 hours AND
2. All symptoms of overdose must be resolved before discharge

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.

If the MMT physician is uncertain about appropriate management, contact the IWK Regional Poison Control Center immediately.

IWK Regional Poison Control Center
Tel: 1-800-565-8161
Website: www.iwkpoisoncentre.ca

11.3 Refusal to Go to Emergency Department

If the patient refuses to go the emergency department, then it may be necessary to fill out a Form 2, under Sections 8 and 9 of the Nova Scotia *Involuntary Psychiatric Treatment Act* (2005), which allows an involuntary psychiatric assessment of the patient at an emergency department. The patient will have to be medically cleared by the emergency physician prior to being seen by the psychiatrist.

Many MMT physicians are reluctant to complete a Form 2 on a patient who is alert and coherent. However, methadone overdose meets the requirements for an involuntary assessment.

Methadone overdose meets the requirements for an involuntary assessment because:

1. The patient is at imminent risk of bodily harm.
2. The patient has a mental health diagnosis (addiction) and as the result of the mental disorder, the person is likely to suffer serious physical impairment or serious mental deterioration. This disorder can make it difficult for the patient to appreciate the need for medical treatment. (Clinical experience suggests methadone patients tend to be far more concerned about methadone withdrawal than intoxication. The MMT patient might be worried that they will receive naloxone in the emergency department or that their next methadone dose will be reduced or delayed).

If the patient refuses to go to the emergency department and a clinical decision is made to not complete a Form 2 (e.g., no MMT physician available onsite or the MMT physician is speaking to the patient by phone and has not assessed the patient in the preceding 72 hours as required by a Form 2), then it is reasonable to send an ambulance or police to the patient's home.

If the MMT physician decides not to complete a Form 2 or to call emergency services, the patient should be asked to sign an AMA or "Against Medical Advice" form (See Appendix O: Against Medical Advice (AMA)). 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.

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.

Overview

Opioid-dependent women are at increased risk of obstetrical and medical complications due to repeated cycles of opioid intoxication and withdrawal. Opioid-dependent women have higher rates of premature delivery and infants with low birth weight leading to higher rates of infant morbidity and mortality.[142-151] 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.[152,144, 151]

MMT is considered the treatment of choice for pregnant women for opioid dependency. 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.[153-154, 151] Respect and a non-judgmental approach are critical. Guilt and shame about substance use, fear of being judged and of having children removed are major barriers to care. A respectful approach acknowledges that change is a process and meets women at their stage of change. Preserving the mother-infant bond is important. Support encompasses the mother-child unit and each woman is respected as a mother, even when she is separated from her child.

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

STANDARDS

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

GUIDELINES

1. MMT physicians should ensure pregnant opioid-dependent patients are counselled 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 consider consultation with a physician who is experienced in MMT in pregnancy when contemplating initiating a pregnant patient on methadone maintenance for opioid dependence.
4. The MMT physician should aim for a maintenance dose of methadone that keeps the patient comfortable for 24 hours and helps maintain abstinence.
5. The MMT physician should assess the daily methadone dose for adjustments, anticipating the need for dose increases during the third trimester of pregnancy to prevent maternal withdrawal symptoms.
6. As an alternative strategy, MMT physicians may consider split dosing during pregnancy if an adequate single daily dose cannot be achieved without side effects as the methadone dose is adjusted upward in the third trimester.
7. The MMT physician should consider dose replacement after reported emesis in pregnant patients in accordance with Section 5.10 Vomited Doses.
8. The MMT physician should encourage pregnant patients to continue methadone maintenance therapy during pregnancy.

9. The MMT physician should only consider tapering and detoxification in patients demanding it and after reviewing significant risks based on clinical and social stability, previous good response to tapering, and the absence of concurrent psychiatric disorders or addiction to other substances.
10. The MMT physician should assist the MMT patient in obtaining adequate prenatal care by referring for obstetrical care as soon as pregnancy is identified.
11. The MMT physician should ensure that there is open communication between the methadone and obstetrical physician regarding the use of MMT during pregnancy and planning for labour and delivery.
12. During labour and delivery, the MMT physician should ensure the pregnant MMT patient receives her regular daily methadone dose.
13. The MMT physician should monitor the MMT patient closely for symptoms of methadone intoxication and mood disorders during the postpartum period.
14. The MMT physician may need additional visits with the patient during the immediate postpartum period to provide support during this transition phase.
15. The MMT physician should encourage breastfeeding during MMT.
16. The MMT physician should consider referring to a child protection agency, depending on the mother's length of time in treatment, the stability of substance use, and social situation, according to provincial legislation.

12.1 Effects of Methadone on the Neonate

To date, no conclusive long-term study has been published about the long-term effects of neonatal exposure to methadone.[155-159] Environmental factors and caregivers can play a significant role in mediating these effects of methadone exposure on infants' growth and development.

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.[160-161]

The most significant risk of methadone exposure during pregnancy is neonatal withdrawal also known as neonatal abstinence syndrome (NAS).[162]

Up to 85% of newborns exposed to methadone experience withdrawal symptoms and signs[163-164] **such as:**

1. Central nervous system (CNS) hyperirritability (i.e., high-pitched cry, increased muscle tone, sleep disturbances, tremors, seizures)
2. Gastrointestinal dysfunction (i.e., poor feeding, regurgitation, vomiting, loose stools)
3. Metabolic, vasomotor and respiratory disturbances (i.e., sweating, recurrent sneezing, yawning, fever)

Withdrawal usually begins within 72 hours of birth, but late presentations (up to 2 to 4 weeks after birth) have been reported,[165] and symptoms may last for several weeks or months. Some infants will require specialist consultation with a paediatrician or neonatologist to assist in managing their opioid withdrawal therapy.

12.1.1 Neonatal Opioid Withdrawal (Neonatal Abstinence Syndrome or NAS)

If withdrawal occurs, the onset of symptoms depends on the half-life of the substance used and when the last dose was taken. The occurrence and severity of neonatal opioid withdrawal does not correlate with higher maternal methadone dose.

Neonatal opioid withdrawal is always a diagnosis of exclusion. When neonatal opioid withdrawal is suspected, other diagnoses such as hypoglycaemia, hypocalcaemia and sepsis should be ruled out first.

Infants of mothers who used prescription drugs during pregnancy, especially benzodiazepines, barbiturates and antipsychotics, as well as alcohol and nicotine, may have neonatal withdrawal symptoms for a longer duration.

Rooming-in with the infant, breast-feeding, frequent skin-to-skin contact and cuddling is encouraged. This increased contact results in a demonstrated reduction in the need to treat opioid-exposed infants.

12.2 MMT During Pregnancy

12.2.1 Inpatient vs Outpatient

There are no studies to demonstrate the efficacy and safety of inpatient over outpatient stabilization. The majority of pregnant women can be started safely as an outpatient. If a pregnant woman complains of uterine irritability (e.g., abdominal cramping and bleeding) during outpatient initiation, hospital admission is indicated.

One advantage of inpatient induction is that, if required, it allows for investigations of maternal health and prenatal status and referral to others (e.g., social worker, obstetrical care provider).

Early referral for prenatal care is essential. Any opioid-dependent pregnant woman is considered to be high-risk.

12.2.2 Methadone Dosing During Pregnancy

Protocol for inpatient induction:[166-167]

1. Methadone induction should begin at the first sign of withdrawal. Based on our experience, the expected length of stay is approximately 5 to 7 days.
2. On Day 1: Provide 10-20 mg of methadone as an initial dose at onset of withdrawal symptoms, followed by supplemental 5 mg every 4 to 6 hours if withdrawal symptoms are present.
3. On Day 2: Provide previous day's total dose as a single morning dose, followed by supplemental 5 mg doses every 4 to 6 hours for withdrawal symptoms.
4. On Subsequent Days: continue as above until comfortable on 1 daily dose with no supplemental medications over a 24-hour period.
5. Subsequent dose increases will be needed as outpatients.

Protocol for outpatient induction:

Outpatient methadone induction during pregnancy should be managed according to the same induction schedule described in Section 5.4 The Initial Methadone Dose.

12.2.2.1 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.[168-171] Therefore, the risks of illicit opioid use outweigh the potential risks of higher methadone doses in such situations.

12.2.2.2 Dose Adjustments During Pregnancy

If on methadone prior to conception, women in MMT can continue on their pre-pregnancy dose during the first and second trimesters.[166] Methadone clearance rates gradually increases from the first to the third trimester, resulting in lower mean serum methadone levels as the pregnancy progresses.[172-174] 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.[175-176] Small increments in methadone dose later in pregnancy may be required.

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 (See Section 7.2 Take-Home Doses: Criteria) for take-home doses or arrangements can be made with the pharmacy to provide an evening observed dose. 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.[176, 177] Split dosing should be done in collaboration with a methadone prescriber with experience in prescribing methadone for pregnant women.

12.2.2.3 Managing Vomited Doses

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 clinic staff did not observe emesis (See Section 5.10 Vomited Doses).

12.3 MMT Tapering or Withdrawal During Pregnancy (Prenatal Methadone Withdrawal Management)

The standard of care for pregnant opioid-dependent patients is methadone maintenance throughout pregnancy and postpartum. However, some patients insist on detoxification from all drugs during pregnancy. Patients insisting on withdrawal or tapering should be informed that the risk of relapse with dose reduction or discontinuation of methadone in pregnancy is high – certainly no less than in non-pregnant patients.

The patients who are most likely to be successful in withdrawal during pregnancy and to remain drug-free are those who have had prolonged stability on methadone, have had drug treatment including relapse prevention and are socially stable.

Patients should also be made aware of all the risks of being in withdrawal when pregnant.

There is limited guidance in terms of the rate of methadone tapering or detoxification. The dose should be decreased slowly by no more than 5 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.

12.4 Prenatal Care for MMT Patients

The addition of on-site prenatal care has been shown to improve attendance and pregnancy outcomes.[153] Certain studies show that methadone substitution treatment provides pregnant women with greater social stabilization and prenatal care.[178] Therefore, comprehensive care, which provides MMT and prenatal care, is the most effective approach in increasing patient retention and reducing adverse neonatal outcomes.[179]

12.5 Intrapartum Management for MMT Pregnant Patients

Methadone will not provide pain relief during labour and additional analgesia will be required. Thus methadone should not be used as pain control in labour. The regular methadone dosage should be continued and not considered as part of the pain management plan. The usual labour and delivery pain medication can be used. Epidural anesthesia is usually the preferred method of pain control in labour, due to altered pain perception in this population group. Nitrous oxide may be useful in the second stage. Opioid analgesics may be used, but the dose may need to be higher than expected for a non-opioid-dependent woman. The patient-must be monitored for somnolence and respiratory depression.

When pregnant women who are already on methadone arrive at a hospital in labour, the usual methadone dose can be given in a decreased volume of fluid (by arrangement with the pharmacy). If oral fluids are contraindicated, methadone may be replaced by intravenous opioid management. Mixed agonist-antagonists must be avoided as they can precipitate acute withdrawal symptoms.

Sensitivity is needed during intrapartum and postpartum pain management. Many women who use substances have experienced sexual trauma and Post Tramatic Stress Disorder (PTSD). Vaginal exams or the pain of childbirth can trigger symptoms, which in turn may cause intensification of labour pain.

12.6 Postpartum Management for MMT Patients

12.6.1 Dosing

A few weeks postpartum, the MMT patient may find her established dose of methadone is too high, in particular if the dose was increased in the third trimester. If this occurs, the dose should be decreased based on clinical symptoms until a new stable dose is reached. For those women whose dose was split, a split dose may no longer be required. The MMT physician should consider the risk of relapse to illicit opioids prior to beginning the decrease. Any decrease in dose should be based on clinical assessment.

12.6.2 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, attendance at drop-in centers, and parenting classes should be encouraged.

12.6.3 Breastfeeding

Methadone enters the breast milk in very small amounts that are unlikely to be clinically significant.[180-181] The mean daily amount of methadone ingested by infants ranges between 0.01-0.05 mg depending on the maternal methadone dose. This amount is not sufficient to prevent NAS and the infant still requires additional opioid treatment for NAS. Breastfeeding is contraindicated in the presence of active substance abuse.

12.6.3.1 Breastfeeding and Hepatitis C and HIV

No studies have demonstrated transmission of Hepatitis C (HCV) through breast milk alone to infants.[182] Breastfeeding by women who are infected with HCV is considered safe. Breastfeeding is contraindicated if patients are HIV-positive.

12.7 Reporting to Child Protection Agencies

In Nova Scotia, the *Children and Family Services Act S.N.S 1990, c.5*. outlines a legal responsibility to promote the well-being and protection of children. 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 open and informed decision-making by child protection authorities.

Consider immediate referral if the pregnant woman has children in her care and there is a child protection concern.

13. MMT in Federal/Provincial Correctional Facilities

Incarcerated opioid-dependent individuals should be offered ongoing MMT or initiation of MMT.

Overview

Incarcerated opioid-dependent individuals should be offered ongoing MMT or initiation of MMT. High-risk behaviour such as injection opioid use can be seen within correctional facilities. The prevalence of HIV and viral Hepatitis is high in the correctional population due in part to the prevalence of needle sharing. The controlled environment, imperatives for security, and the governance of correctional policy may affect the institutional MMT physician's ability to provide patient-centered care at community standards. The trusting and non-judgmental therapeutic relationship between MMT physicians and patients must remain the focus of treatment.

STANDARDS

1. The institutional MMT physician shall ensure a Treatment Agreement (See Appendix E: Sample Methadone Maintenance Treatment Agreement) is signed by the patient.
2. The institutional MMT physician shall ensure the Treatment Agreement (See Appendix E: Sample Methadone Maintenance 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. Naloxone (NARCAN®) must be available.
5. The institutional MMT physician shall ensure arrangements are made for methadone pick-up at a community pharmacy in the event of an outside pass.
6. 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.
7. The institutional MMT physician shall not prescribe take-home doses to a patient upon release from the correctional facility.

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 behaviour at the onset of treatment.
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 assess patients in person or via telemedicine for dose increases.
8. In exceptional circumstances due to facility constraints, (e.g., lockdown or inmate movement issues) when the institutional MMT physician cannot assess a patient, the institutional MMT physician should designate a nurse to assess the patient for dose increases. A single dose increase of no more than 10 mg

can be given by the nurse prior to the assessment of the facility physician.

9. The institutional MMT physician should ensure a process is in place for the safe administration of methadone for patients.
10. The institutional MMT physician should ensure a safe process is in place to initiate patients on MMT, if feasible.
11. The institutional MMT physician should ensure every effort is made to provide continuity of care with a community physician.
12. Prior to release from the facility, the institutional MMT physician should slowly decrease (taper) the methadone dose if the patient is going to a community with no available MMT physician. This should be done only as a last resort.
13. 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.
14. The institutional MMT physician should ensure counselling and support is provided throughout the involuntary taper process and that the opportunity for the patient to reapply for MMT is available, if they can adhere to program requirements.

13.1 Approaches to Treatment in a Correctional Facility

13.1.1 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 counsellors (where available), and persons responsible for the patient's MMT in the community. The importance of ongoing communication between the community methadone prescriber and the institutional physician cannot be overstated, particularly at the time of incarceration and at the time of release.

Patient confidentiality is extremely important in health care, and that should apply to the correctional system as well. Doctor-patient confidentiality must be maintained, as with any health care encounter.

13.1.2 UDS

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

13.1.3 Missed or Vomited Doses

Refer to Section 5.10 Vomited Doses and Section 5.8 Summary of Managing Missed Doses

13.2 Continuing Ongoing MMT

13.2.1 Issues Unique to Providing MMT in Correctional Facilities

13.2.1.1 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 (then methadone should be discarded or even returned to prescribing pharmacy to allow for the "bottles" to be accounted for by pharmacy).

13.2.1.2 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 (See Appendix E: Sample Methadone Maintenance Treatment Agreement).

13.2.1.3 Dosing on Admission

Upon admission to the correctional facility and prior to dispensing the first methadone dose, confirmation must be obtained about whether a patient is enrolled in and attending a community MMT program and receiving community methadone maintenance.

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. The time and dosage of the last witnessed methadone ingestion should be determined. A physician may delegate a nurse to assess the patient (vital signs, appearance and level of alertness, intoxication, symptoms of withdrawal, date of last observed ingestion, communication with community provider if available, recent medical and psychosocial history and results of UDS) to recommend continuance of MMT at the same dose. The institutional MMT physician may then provide 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.

To provide safe MMT, institutional MMT physicians must use their clinical judgment to determine the appropriate dose. If there is suspicion of missed or reduced doses, a portion of the stated dose may be given (See Section 5. Dosing During Induction, Stabilization and Maintenance). If it can be confirmed that the patient has been on a stable dose, this dose should be maintained while they are incarcerated. If the dose is reduced, the institutional MMT physician should reassess the patient more frequently for symptoms of withdrawal and intoxication, and appropriate dose changes should be made. Benzodiazepines should be used very cautiously, if at all. If the patient is on other sedating medications they should be monitored closely until the institutional MMT physician has done an appropriate assessment. If the dose is withheld based on the initial nursing assessment, the patient should be assessed by the attending physician without unreasonable delay.

13.2.1.4 Delegated Dose Increases

If the institutional MMT physician cannot assess an inmate (e.g., in exceptional circumstances such as lockdown or offender movement issues), the institutional MMT physician should delegate a nurse to assess a patient for dose increases.

Prior to the assessment of the institutional MMT physician, a single dose increase (of no more than 10 mg) can be given by the nurse.

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

1. The reason the assessment is being performed by the nurse and not the physician
2. Any obvious signs of withdrawal noted by the nurse
3. When the withdrawal symptoms begin in relation to the dose (e.g., 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. Signs and symptoms of sedation
9. Any ongoing opioid use (drug name, amount used, and route of use)

13.3 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:

1. MMT patients to show proper identification
2. MMT patients receiving methadone should be isolated from other patients during administration process
3. Drink water following administration
4. Nurse can inspect mouth before and/or after
5. No wearing of bulky clothing (e.g., parkas, hoodies)
6. No bringing cups or containers into the administration area
7. Frisking MMT patients before entering and/or upon leaving administration area
8. Limit access to water post ingestion (e.g., fountains, bathrooms)
9. A 20-minute direct observation should follow immediately

13.4 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. Contact with the NSPMP is advised to obtain a patient profile before initiation or resumption of MMT in a correctional facility.
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 and Section 5. Dosing During Induction, Stabilization and Maintenance).
5. Pregnant patients currently using opioids must be offered MMT while incarcerated.
6. Patients with HIV infection, or Hepatitis B or C should be made a high priority for being offered methadone treatment while incarcerated.
7. Consideration should be given to discharge planning and arrangements for a community MMT provider upon release.

13.5 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 available in all correctional facility health centres.

13.6 Out-of-Facility Pass

The institutional MMT physician shall ensure that arrangements will be made such that methadone be available in the event of an outside pass.

13.7 Treatment Planning for Release

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

13.7.1 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.

13.7.2 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 health care 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.
3. Contact the community methadone provider.

If a patient is released without a community MMT physician, every effort should be made to find one for the patient by contacting the Methadone Program at the CPSNS.

If assistance is required by the facility in finding a local pharmacy that dispenses methadone, contact the Nova Scotia College of Pharmacists.

13.8 Take-Home Doses

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

13.9 Involuntary Withdrawal

Refer to Section 8.2 Involuntary Withdrawal.

14. Hospital-Based MMT

In many cases, hospital physicians know little about MMT and must rely on the expertise of an MMT physician.

Notable Definitions

Attending Physician (or Most Responsible Physician [MRP])
The physician who is responsible for the overall care of the patient, and who must approve all orders written by other physicians. Physicians without a methadone exemption are not allowed to order or prescribe methadone unless they receive a special exemption from Health Canada.

Hospital MMT Physician
The physician who prescribes methadone. This physician holds the appropriate general exemption to prescribe methadone and is usually a different physician than the MRP. For example, when a patient on a stable dose of methadone is admitted to the hospital with pneumonia, the attending physician will manage the pneumonia and the hospital MMT physician will order the methadone.

Temporary Methadone Exemption
If the attending physician does not hold a methadone exemption for dependence, and there is not an MMT physician within the hospital available to manage the methadone for this particular patient during their inpatient stay, the attending physician can contact Health Canada, Office of Controlled Substances, Methadone Program at (613) 946-5139 or toll free at (866) 358-0453 to obtain a temporary exemption to treat this patient while a hospital inpatient. The physician must provide their full name, license number, telephone number, the name and address of the hospital, the patient's full name, age and sex and the required methadone dose. The physician must also provide the date the order for methadone was written and the telephone number of the hospital pharmacy. Temporary exemptions are only valid for one specific patient, and only for the duration of that patient's stay in hospital. Temporary exemptions are only granted for the care of patients who are already on methadone at the time of admission. Dosage adjustments during hospitalization should generally be made in consultation (informal or formal) with an experienced MMT provider holding the appropriate general exemption where it is available. In the case of suspected methadone toxicity, a dose decrease may need to be implemented before consultation is obtained.

Overview

General or psychiatric hospitals should identify at least one methadone physician, on staff or in the community, who has agreed to be available for telephone consultations. Collaboration with patient's current community MMT prescriber by telephone or in person is strongly recommended. If feasible, the community methadone physician should be encouraged to seek out active hospital privileges so that he/she may write hospital orders for methadone.

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

STANDARDS

None for this section.

GUIDELINES

1. General hospitals should have access to at least one MMT physician who is on their medical staff and available for consultation. Methadone should be on the hospital formulary.
2. The hospital MMT physician should verify the patient's current dose and date it was last dispensed with the patient's pharmacy (i.e., current methadone dose, recent changes in dose, missed doses, number of take-home doses per week, and exact date and time of the last reported dose and last witnessed dose).
3. The hospital MMT physician should ensure the prescription at the community pharmacy is cancelled for the duration of the patient's hospital stay.
4. The hospital MMT 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 hospital methadone order should specify that the dose be mixed in orange Tang or other crystaline juice, and dispensed daily with witnessed ingestion 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 NPO, the hospital MMT physician may allow the methadone to be mixed in water (or clear juice, with the attending physician's approval) to a final volume of 15 ml.
7. The hospital MMT physician should prescribe oral or parenteral opioids to minimize withdrawal symptoms if methadone is not available or is contraindicated (e.g., prolonged QTc interval).
8. To avoid methadone toxicity, the hospital MMT 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. 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. In patients who are already on methadone, are currently getting take-home doses and are going to start daily witnessed ingestion with admission to hospital, consideration should be given to potential for overdose if there is any concern of not having regularly ingesting their full dose while they have been in the community with take-home doses. The involvement of an experienced MMT physician, with a long-term dependency exemption, is advisable in any of the preceding situations.
10. On discharge, the hospital MMT 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).

14.1 Guidelines for Hospital Pharmacies and Medical Administrators

All hospitals are expected to have methadone on their formulary. If methadone is not on the formulary, the hospital should have a process in place to safely and timely secure methadone. A community pharmacy may deliver methadone to the hospital. Methadone should be stored in a locked narcotic cupboard and dispensed under the supervision of a nurse.

14.2 MMT Physicians Working in a Hospital

14.2.1 Verifying the Community Dose

It is not safe to rely solely on the patient's history. Only the dispensing pharmacist is able to verify with certainty whether the patient has filled their methadone prescription and when it was last dispensed.

The history of the last witnessed ingestion is important. The community MMT prescriber can verify the prescribed dose only. Please refer to usual community standards for methadone maintenance. 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 drug screening, including methadone, may be useful. The hospital MMT physician should cancel the methadone prescription at the community pharmacy for the anticipated duration of the hospital stay.

14.2.2 In-Hospital Assessment of the Patient

A focused assessment will identify acute risk factors for 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 reported dose and last witnessed dose
- Recent substance use (including alcohol)

Chart Review

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

Investigations

- Baseline UDS
- ECG

14.2.3 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.

14.2.4 Patients on "Nothing by Mouth" (NPO)

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. On days of surgery, the usual amount of methadone should be given in small amount of juice (i.e., 10-15 ml) in consultation with the anaesthesiologist.

14.2.5 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 or that prolong QTc interval (See Appendix A: Drug to Drug Interactions and Appendix H: Medications that Cause Prolonged QTc Interval)
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 be withheld if the patient shows signs of sedation or intoxication.

When adjusting the dose, the hospital MMT 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.[183-184] 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.

14.2.6 Initiating MMT in Hospital

The treating physician must involve a MMT physician with a long-term dependency exemption to initiate MMT in hospital for pregnant patients, and for seriously ill patients who require prolonged hospitalization and who might leave against medical advice. If MMT initiation is required, the treating physician must consult with a community MMT prescriber holding the general methadone exemption for dependence.

14.2.7 Opioid Withdrawal Management

If it is determined, for medical reasons or patient preference, that opioid withdrawal management is indicated, the treating physician should consult with an addiction physician experienced in withdrawal management.

14.2.8 Discharge from Hospital

There should be adequate communication between the hospital MMT physician and the prescribing community MMT physician, and community pharmacist at the time of discharge.

Upon discharge from hospital, it may be necessary in some cases, to allow take-home doses in order for the patient to recover from their illness or surgery at home. However, the decision to prescribe take-home doses should be made by the community MMT physician as soon as it can be arranged.

This needs to be considered when prescribing methadone within the first few days of admission, the treating physician should be aware most patients act responsibly with take-home doses, but there is also the risk of diversion or not having taken the complete dose.

When issuing a multiple day or weekend pass, the patient should only be issued take-home doses if they had been on take-home doses prior to admission. The community pharmacist should be contacted for the history of an observed dose/witnessed ingestion.

Appendices

Appendix A: Drug to Drug Interactions

Pharmacodynamic

Pharmacodynamic interactions involve drugs that cause additive effects to undesired side effects of methadone such as:

- Medications that cause sedation including alcohol, benzodiazepines, barbiturates, and dimenhydrinate. The combination of these drugs with methadone results in a high risk of toxicity and overdose during induction and risk of CNS depression during maintenance.
- Medications that cause constipation and urinary retention through their anticholingergic effects
- Medications that cause QTc prolongation (See Appendix H: Medications that Cause Prolonged QTc Interval)

Pharmacokinetic

Pharmacokinetic interactions involve drugs which interact with the metabolism of methadone and thereby increase or decrease the expected methadone levels and subsequent effects; or drugs whose metabolism and subsequent blood levels are affected by methadone. Most of these interactions involve the cytochrome P450 (CYP450) enzymes. While there are more than 28 CYP enzymes,[185-186] the most important enzymes in methadone metabolism are CYP3A4 and CYP2B6. Some P450 interactions may be potential (i.e., theoretical), others are currently being investigated to confirm their clinical significance.[187] The MMT physician should remain aware of how methadone may affect the metabolism of other drugs.

Drugs metabolized by one or more CYP enzymes are termed substrates. An **inhibitor** is any drug that slows the metabolism via specific CYP enzymes resulting in a less rapid metabolism of substrate drugs, which may result in higher than expected levels of substrate drugs. An **inducer** is any drug that 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. Drugs and substances that increase and decrease the effects of methadone are listed in the table below.

		Increase methadone effect	Decrease methadone effect
Anti-infection	Antibacterial	Ciprofloxacin (Cipro) Clarithromycin (Biaxin) Erythromycin	**Fusidic Acid (Fucidin)**
	Antifungal	Fluconazole (Diflucanl) Ketoconazole (Nizoral)	
	Antimalarial		**Rifampin**
	Antiretroviral	Delaviridine (Resriptor)	**Abacavir (Ziagen)** **Amprenavir (Agenerase)** **Efarvirenz (Sustiva)** **Lopinavir/Ritonavir (Kaletra)** **Nelfinavir (Viracept)** **Nevirapine (Viramune)** **Ritonavir**
Cardiac	Ca++ channel blocker	Verapamil (Isoptin)	
Corticosteroid			**Dexamethasone (Decadron)**
Gastrointestinal	Antacid	Cimetdine (Tagamet) Omeprazole (Losec)	

		Increase methadone effect	Decrease methadone effect
Neurologic	Anti-alcohol	Disulfiram (Antabuse)	
	Anticonvulsant		**Carbamazepine (Tegretol)** **Phenytoin (Dilantin)**
	Migraine	Dihydroergotamine (Migranal)	
Psychiatric	Antianxiety	Diazepam (Valium)	
	Antidepressant	Fluoxetine (Prozac) Fluvoxamine (Luvox) Moclobemide (Manerix) Nefazodone (Serzone) Paroxetine (Paxil) Sertraline (Zoloft)	
	Barbiturate		**Amobarbital (Amytal)** **Butalbital (In Fiorinal)** **Pentobarbital (Nembutal)** **Phenobarbital** **Secobarbital (Seconal)**
Opioids			**Butorphanol (Stadol)*** **Buprenorphine (Subutex)*** **Fiorinal (Due To Butalbital)** **Naloxone (Narcan)*** **Naltrexone (Revia)*** **Nalbuphine (Nubain)*** **Pentazocine (Talwin)***
Urologic	Diuretics		**Spironolactone (Aldactone)**
	Urinary acidifiers		**Vitamin C (In Large Doses)** **K-Phos**
	Urinary alkalizers	Sodium Bicarbonate Potassium Citrate (Polycitra, K-Lyte)	
Herbal drugs		Cat's Claw Chamomile Echinacea Goldenseal	**St. John's Wort**
Food		Grapefruit Juice	
Addictive drugs		Alcohol (Acute Use)	**Alcohol (Chronic Use)** **Cocaine** **Heroin** **Tobacco**

* These opioids are contraindicated. They are either pure antagonists or agonist/antagonists and will cause acute withdrawal if given to a patient on methadone maintenance.

The following websites may be consulted:
www.atforum.com/SiteRoot/pages/addiction_resources/Drug_Interactions.pdf
http://www.hivclinic.ca/main/drugs_interact.html

Appendix B: Sample 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. The following safety measures, methadone dispensing practices, and clinic policies have been discussed 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 crystaline juice in front of the pharmacist. **The ingestion of methadone must be witnessed 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 3 or more doses are missed in a row, the methadone dose must be withheld from the patient to prevent an overdose.** The patient must be reassessed by the methadone physician before methadone is restarted.
- If there is any evidence of intoxication, sedation or impairment (slurred speech, stumbling gait, disorientation) the methadone dose must be withheld 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 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, no take-home doses may be released until the physician reauthorizes.
- If the pharmacist observes evidence of an overdose, the patient will be advised that urgent medical care is required. 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.
- Take-home doses should be dispensed 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 locked box be presented prior to issuing take-home doses.

- Any doses of methadone vomited can only be replaced if the pharmacist or a member of the pharmacy team has witnessed the vomiting within 30 minutes of ingestion, informs the methadone provider of such, and the physician provides a written prescription for the replacement dose.
- The pharmacist or methadone physician may request that take-home dose bottles be returned to the pharmacy. The MMT patient shall return all take-home dose bottles to the pharmacy before receiving the next take-home doses.
- 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. Regardless of doses that may end up not being dispensed, the prescription is not to be dispensed after the end date.
- A patient is authorized 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 *NSCP MMT Standards of Practice* and the *CPSNS Methadone Maintenance Treatment Handbook* have been exhausted, and then only in accordance with these documents.

Thank you, _____

Appendix C: 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
Download application PDF here
Website: http://www.hc-sc.gc.ca/hc-ps/pubs/precurs/meth_on-eng.php

College of Physicians and Surgeons of Nova Scotia Methadone Program
Tel: (902) 421-2216

Nova Scotia Prescription Monitoring Program
Toll-free: 1-877-476-7767
Website: www.nspmp.ca/contact.php

IWK Regional Poison Centre
Emergency Telephone Number: 1-800-565-8161 (within NS and PEI only)
Tel: (902) 470-8161 (Halifax or outside NS and PEI)
Website: www.iwkpoisoncentre.ca/pub_contact.html

Nova Scotia College of Pharmacists
Tel: (902) 422 8528
Website: www.nspharmacists.ca/contactus/index.html

Methadone Drug Interactions Information
Website(s): www.atforum.com and /or www.drug-interactions.com

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

Regional Addiction Services

Health Authority	Location	Contact Number
Capital Health Website: www.cdha.nshealth.ca/addiction-prevention-treatment-services	Central intake	(902) 424-8866
South Shore Website: www.southshorehealth.ca/home-community/addiction-services.html	Lunenburg Bridgewater Liverpool	(902) 634-7325 (902) 543-7882 (902) 354-3422
South West Website: www.swndha.nshealth.ca/pages/addictions.htm	Yarmouth Barrington Passage Digby Shelburne Clare Medical Health Centre	(902) 742-2406 (902) 637-1432 (902) 245-5888 (902) 875-8645 (902) 645-3502
Annapolis Valley Website: www.avdha.nshealth.ca/program-service/mental-health-addiction-services	Kings County Middleton Annapolis Royal Wolfville	(902) 679-2870 (902) 825-4825 (902) 365-1701 (902) 542-6302
Colchester East Hants Website: www.addictionservices.ns.ca	Elmsdale Truro Opiate Treatment Program	(902) 883-0295 (902) 893-5900 (902) 893-4776
Cumberland County Website: www.addictionservices.ns.ca	Amherst Springhill Withdrawal Management	(902) 667-7094 (902) 597-8647
Pictou County Website: www.addictionservices.ns.ca	New Glasgow Withdrawal Management	(902) 755-7017 (902) 485-4335
Guysborough Antigonish Strait Website: www.kids1st.ca/businesses/addiction-services-antigonish-guysborough-antigonish-strait-regional-health-authority		1-888-291-3535
Cape Breton Website: www.cbgasha.com	Central Intake Withdrawal Management Opiate Recovery Program	(902) 563-2718 or (902) 563-2583 (902) 563-2040 (902) 794-5465

Appendix D: Diagnostic Criteria for Substance Dependence

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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
   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 E: Sample Methadone Maintenance Treatment Agreement

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.

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.

Sample Methadone Maintenance Treatment Agreement

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 doctor can help you if they happen. If you take the methadone the way your doctor tells you to, the methadone probably won't give you any more problems than that.

14. If your doctor thinks that the methadone is not working for you, the 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 doctor to explain them to you.
2. If a 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 doctor changes your dose of methadone. Your 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 clinic, you are expected to let a clinic 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 doctor or the methadone clinic 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 clinic 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, the clinic 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, the clinic may give you fewer take-home doses of methadone, or it might not let you take methadone home at all.

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 clinic may not give you methadone. If you don't understand these things, ask your doctor to explain them to you.

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 ago

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.

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 the clinic or near the clinic, or do anything else that is illegal
4. Shout, swear, fight or argue in the clinic or anywhere near the clinic
5. Ask people for money in the clinic or near the clinic
6. Break, damage, or steal anything in the clinic or near the clinic
7. 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 the people at the methadone clinic do the following things:

1. Let your methadone doctor give the Nova Scotia Prescription Monitoring Program (NSPMP) your name, date of birth, health card number, address, and the date you started taking methadone. The NSPMP will keep this information private.
2. Let your methadone doctor talk to other doctors or health workers about your care.
3. Let the clinic pharmacist and nurses talk to pharmacists or other health workers to check on how much methadone you were given at another place.

Confidentiality

Everything you tell the clinic staff will be kept private, unless someone who works at the 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. There is a law that makes the clinic 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.

_____	_____	_____
Dated (dd/mm/yyyy)	Patient's Name	Patient's Signature
_____	_____	_____
Dated (dd/mm/yyyy)	Doctor's Name	Doctor's Signature

Appendix F: Sample Initial Patient Assessment Form

Sample Initial Patient Assessment Form			
Name	**Age**	**Date**	
Expectations of / Goals for MMT – Why treatment?			
Drug of Choice		**Second Drug of Choice**	
Addiction History: *c=current (past 3 months) p=past* *Include all: opioids, alcohol, benzodiazepines, cocaine, amphetamines, prescription stimulants, hallucinogens, solvents, tobacco, cannabis, steroids*			
Substance/first use		Route/progression/typical amount/frequency	Last use
	c		
	p		
	c		
	p		
	c		
	p		
	c		
	p		
	c		
	p		
	c		
	p		
	c		
	p		
Addiction History			
How started drug use			
How started opioid use			

Sample Initial Patient Assessment Form

Length of opioid addiction			
Drug Attitudes			
What likes about opioid use			
What dislikes about opioid use			
Perceived control over drug use:	yes ❒	no ❒	
Triggers			
Drug Behaviour			
Needle injections a day: current		At peak use	
Needle source			
Opioid source: current		At peak use	
Opioid prescriptions: current			
Past			
Money spent a day on drugs: current		At peak use	
Source of money for drugs: current		At peak use	
Typical day (time getting, using, recovering from drugs)			
Current			
At peak use			
Risk behaviours: current			Needle sharing Crime Driving Safe sex Sex work
Past			
DSM Criteria			
Need for increasing dose over time:	yes ❒	no ❒	
Used more than planned:	yes ❒	no ❒	
Drug overdoses:	yes ❒	no ❒	
Hospital admissions or other significant health consequence resulting from drug related illness:	yes ❒	no ❒	
Presence of withdrawal symptoms: (dysphoria, insomnia, myalgia, lacrimation/rhinorrhea, sweating, piloerection, papillary dilation, nausea/vomiting/diarrhea).			
Addiction Treatment			
Attempts to cut down or stop:	yes ❒	no ❒	
How tried to cut down or stop			
Past treatment of addiction			detox structured treatment program 28 day Offender Substance Abuse Program (OSAP) methadone NA/AA

Sample Initial Patient Assessment Form		
Plans for treatment for other current drug problems		
Longest period in full remission		
Factors involved in relapse		
Effect of Drug Use on Life		
Family		
Friends		
Crime		
Housing		
School		
Job		
Physical health		
Mental health		
History of Behaviour Addiction		Gambling, internet, exercise, shopping, sex, eating, work
Immunization	**Date:**	HAV HBV
Current Medications		Prescribed OTC Herbal Contraception Allergies
Current MD's		
Current Medical Problems		HCV HIV Psychiatric

Sample Initial Patient Assessment Form

Past History (admissions)		
Past Transfusions		
History of abuse		
Family History		
Father Sisters	Mother Brothers	Addiction Psychiatric Ischemic heart disease Hypertension Stroke Diabetes Cancer Respiratory (Emphysema/COPD) Neurologic (Parkinson's) Liver
In Women G P TA Miscarriage? Adopted out? First Day of LMP? Menstrual Cycle Characteristics? Current Contraception Method? (Review ↑ risk of pregnancy)		
Social History		
Financial		
Employment		
Education		
Drug plan		
Relationship		
Family		
Children		
Housing		
Legal		
Sexual		

Sample Initial Patient Assessment Form

Review of Systems allergies	**Skin** - tattoos, piercing **Neuro** - vision, weakness, headache, paresthesia **ENT** **CVS** - edema, chest pain, palpitations **Resp** - SOB, cough, Smoking **GI** - pain, swelling Constipation **MSK** - arthralgia, myaqlgia **GU** - hematuria, retention, LMP, birth control **Psych** - depression, sleep, suicidal ideation, anxiety
Fatigue Weight Appetite	
Pain	
Mood	
Smoking: PPD Pack years	
Examination	
BP Weight Height BMI Pulse	
General appearance	
Skin: tattoos Piercing	Spiders Palmar erythema Jaundice
Track marks	
Eyes: pupil size	
ENT	
Teeth	
Thyroid	
Adenopathy	
Neuro	

Sample Initial Patient Assessment Form		
Chest		
CVS	Peripheral edema	
Abdomen	Ascites Liver Spleen	
GU	Testes	
MSK	Dupuytrens	
Psych	Depression	
Formulation	**Start**	**End**
Axis I		
Axis II		
Axis III		
Axis IV		

Sample Initial Patient Assessment Form		
Plan		
• Discuss methadone/buprenorphine benefits and drawbacks		
• Methadone – start date and dose:		
• Initial blood work (CBC, Lytes, AST, ALT, GGT, TBili, ALP, Cr, BUN, Albumin, INR, PTT, FBG, Lipids (TC, TG, LDL,HDL), TSH,) • Pre-test Counselling for HIV, Hep BsAg, Hep CAb, VDRL/RPR +/-bHCG		
• Contract signed		
• Urine drug screen (UDS)		
• Sign release of Info for past records		
• NSPMP profile obtained		
• Psychosocial support plan		

Physician Signature	Date:

Appendix G: 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:

1. Gambling: South Oaks Gambling Screen (Download PDF)
2. Problem Gambling Severity Index (Download PDF)
3. Gamblers Anonymous 20 Questions
4. Sexual Addiction Sexual Addiction Screening Test

Appendix H: Medications that Cause Prolonged QTc Interval

Medications that Cause Prolonged QTc Interval					
System	Class	Risk	Possible risk	Conditional risk	**Avoid with congenital long QT syndrome**
Anti-cancer		Arsenic trioxide Vandetanib	Eribulin Lapatinib Nilotinib Sunitinib Tamoxifen		
Anti-infection	Macrolides	Clarithromycin Erythromycin	Azithromycin Roxithromycin Telithromycin		
	Floxins	Sparfloxacin	Gatifloxacin Gemifloxacin Levofloxacin Moxifloxacin Ofloxacin	Ciprofloxacin	
	Sulfa			Trimethoprim-sulfa	
	Anti-fungals		Voriconazole	Fluconazole Itraconazole Ketoconazole	
	Anti-virals		Amantadine Atazanavir Foscamet	Ritonavir	
	Anti-malarials	Chloroquine Halofantrine			
	Pneumocystis	Pentamidine			
Cardiac	Anti-anginal	Bepridil	Ranolazine		
	Anti-arrhythmics	Amiodarone Disopyramide Dofetilide Ibutilide Procainamide Quinidine Sotalol	Dronedarone Flecainide	Mexilitine	
	Anti-failure				**Dobutamine** **Dopamine**
	Anti-hypertensive		Isradipine Moexipril Nicardipine		
	Diuretic		Indapamide		
	Orthostatic hypoten				**midodrine**
Endocrine	Antilipemic	Probucol			
	Appetite suppressant				**Fenfluramine** **Phentermine** **Sibutramine**
	Somatostatin analog		Octreotide		

Medications that Cause Prolonged QTc Interval					
Gastrointestinal	Anti-emetic	Droperidol	Dolasetron Granisetron Ondansetron		
	Motility modifier	Cisapride Domperidone			
	Antacid		Famotidine		
Immunologic	Anti-allergy				**Epinephrine** **Isoproterenol** **Norepinephrine** **Phenylephrine**
	Antihistamine	Astemizole Terfenadine		Diphenhydramine	
	Immunosuppressant		Tacrolimus		
Musculoskeletal	Muscle relaxant		Tizanidine		
Neurologic	Anti-convulsants		Felbamate Fosphenytoin		
	Parkinson's		Amantadine		
Pregnancy	Labour stimulator		Oxytocin		
	Uterine relaxant				**Ritodrine**
Psychiatric	Anti-psychotics	Chlorpromazine Haloperidol Mesoridazine Pimozide Thioridazine	Clozapine Paliperidone Quetiapine Risperidone Sertindole Ziprazidone		
	Anti-depressants		Venlafaxine	Amitriptyline Citalopram Clomipramine Desipramine Doxepin Escitalopram Fluoxetine Imipramine Nortriptyline Paroxetine Protriptyline Sertraline Trazodone Trimipramine	
	Dementia			Galantamine	
	Mood Stabilizers		Lithium		
	Sedatives		Chloral hydrate		
	Stimulants				**Amphetamine** **Atomoxetine** **Cocaine** **Dexmethylphenidate** **Lisdexamfetamine** **Methylphenidate**

Medications that Cause Prolonged QTc Interval					
Respiratory	Bronchodilator				**Salbutamol** **Levabuterol** **Metaproterenol** **Salmeterol** **Terbutaline**
	Decongestant				**Ephedrine** **Phenylpropanolamine** **pseudoephedrine**
Urologic	Antispasmodic			Solifenacin	**Tolterodine**
	BPH		Alfuzosin		
	Erectile Dysfunction		Vardenafil		

Risk of TdP	Substantial evidence supports the conclusion that these drugs prolong the QT interval and have a risk of TdP when used as directed in labeling.
Possible Risk of TdP	Substantial evidence supports the conclusion that these drugs cause QT prolongation but there is insufficient evidence that they, when used as directed in labeling, have a risk of causing TdP.
Conditional TdP Risk	Substantial evidence supports the conclusion that these drugs prolong QT and have a risk of TdP but only under certain known conditions (e.g. excessive dose, drug interaction, etc.).
Congenital LQTS Risk	Drugs to be avoided, if possible, by patients with Congenital Long QT Syndrome
Females > Males:	Substantial evidence indicates that there is a greater risk of TdP in women (usually > two-fold).

QTc Values:[V]

Women <460 ms
Men <440 ms

Note: Values above 500 ms indicate significant risk of arrhythmia.

V Recommended values source: www.torsades.org, last updated May 1, 2012

Appendix I: Sample Methadone Prescriptions

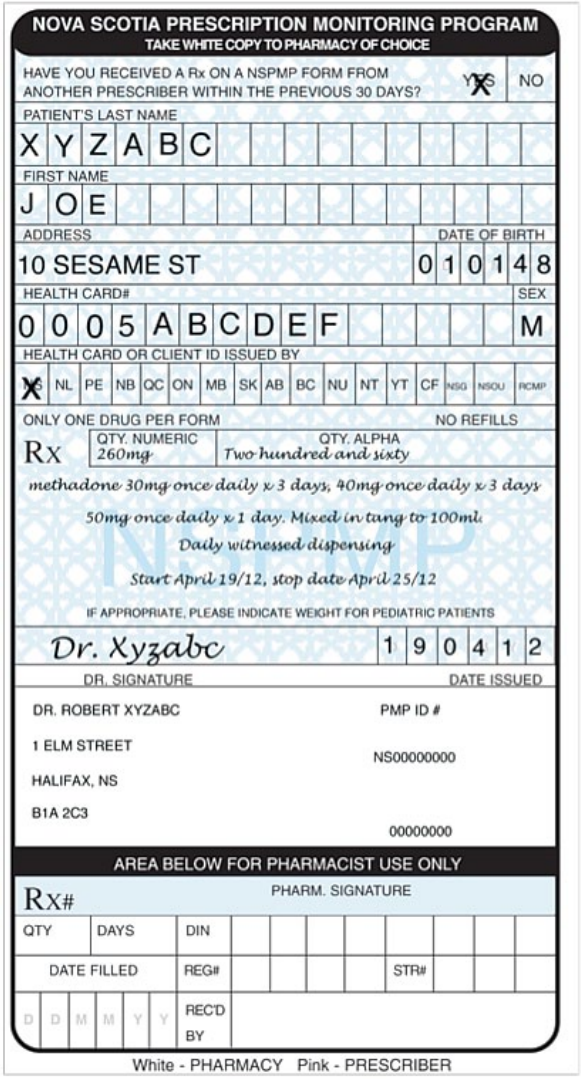
On the methadone prescription, the MMT physician shall specify:

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 recommended 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 if applicable.
5. The start and end date.

Three samples follow to illustrate a prescription with a changing dose, a prescription at a stable dose, and a prescription with take-home doses.

1. Prescription with a changing dose:

This prescription represents a typical induction of methadone, with daily witnessed dispensing of a gradually increasing dose. The prescription must include each dose with the length of time at that dose. The patient requires assessment by the physician or a delegated provider prior to any dose change.



NOVA SCOTIA PRESCRIPTION MONITORING PROGRAM
TAKE WHITE COPY TO PHARMACY OF CHOICE

HAVE YOU RECEIVED A Rx ON A NSPMP FORM FROM ANOTHER PRESCRIBER WITHIN THE PREVIOUS 30 DAYS? YES X NO

PATIENT'S LAST NAME: XYZABC

FIRST NAME: JOE

ADDRESS: 10 SESAME ST

DATE OF BIRTH: 01 01 48

HEALTH CARD#: 0005ABCDEF

SEX: M

HEALTH CARD OR CLIENT ID ISSUED BY: X NL PE NB QC ON MB SK AB BC NU NT YT CF NSG NSOU RCMP

ONLY ONE DRUG PER FORM — NO REFILLS

Rx

QTY. NUMERIC: 260mg

QTY. ALPHA: Two hundred and sixty

methadone 30mg once daily x 3 days, 40mg once daily x 3 days
50mg once daily x 1 day. Mixed in tang to 100ml
Daily witnessed dispensing
Start April 19/12, stop date April 25/12

IF APPROPRIATE, PLEASE INDICATE WEIGHT FOR PEDIATRIC PATIENTS

Dr. Xyzabc — DR. SIGNATURE

1 9 0 4 1 2 — DATE ISSUED

DR. ROBERT XYZABC
1 ELM STREET
HALIFAX, NS
B1A 2C3

PMP ID #: NS00000000

00000000

AREA BELOW FOR PHARMACIST USE ONLY

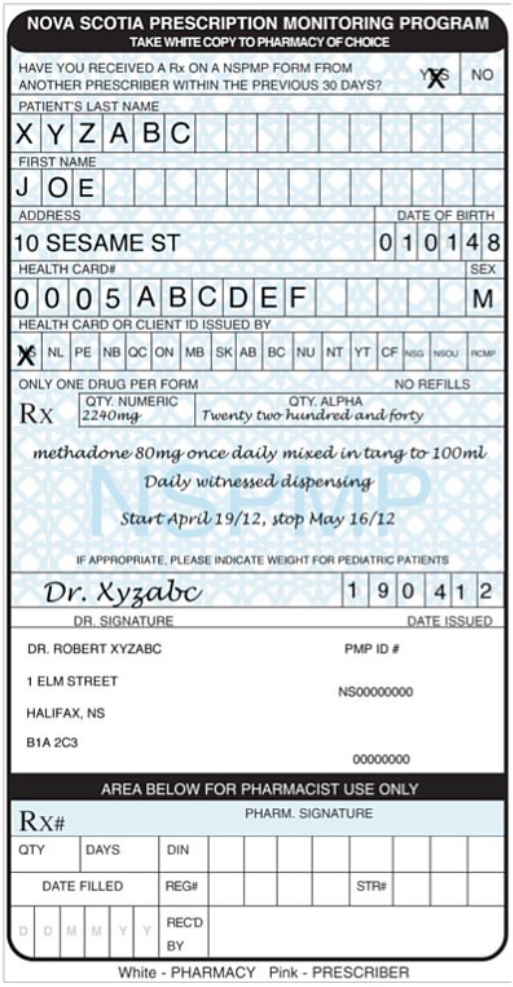
Rx# — PHARM. SIGNATURE

QTY | DAYS | DIN

DATE FILLED | REG# | STR#

D D M M Y Y — REC'D BY

White - PHARMACY Pink - PRESCRIBER



NOVA SCOTIA PRESCRIPTION MONITORING PROGRAM
TAKE WHITE COPY TO PHARMACY OF CHOICE

HAVE YOU RECEIVED A Rx ON A NSPMP FORM FROM ANOTHER PRESCRIBER WITHIN THE PREVIOUS 30 DAYS? YES X NO

PATIENT'S LAST NAME: XYZABC

FIRST NAME: JOE

ADDRESS: 10 SESAME ST

DATE OF BIRTH: 01 01 48

HEALTH CARD#: 0005ABCDEF

SEX: M

HEALTH CARD OR CLIENT ID ISSUED BY: X NL PE NB QC ON MB SK AB BC NU NT YT CF NSG NSOU RCMP

ONLY ONE DRUG PER FORM — NO REFILLS

Rx

QTY. NUMERIC: 2240mg

QTY. ALPHA: Twenty two hundred and forty

methadone 80mg once daily mixed in tang to 100ml
Daily witnessed dispensing
Start April 19/12, stop May 16/12

IF APPROPRIATE, PLEASE INDICATE WEIGHT FOR PEDIATRIC PATIENTS

Dr. Xyzabc — DR. SIGNATURE

DATE ISSUED: 19 04 12

DR. ROBERT XYZABC
1 ELM STREET
HALIFAX, NS
B1A 2C3

PMP ID #: NS00000000

00000000

AREA BELOW FOR PHARMACIST USE ONLY

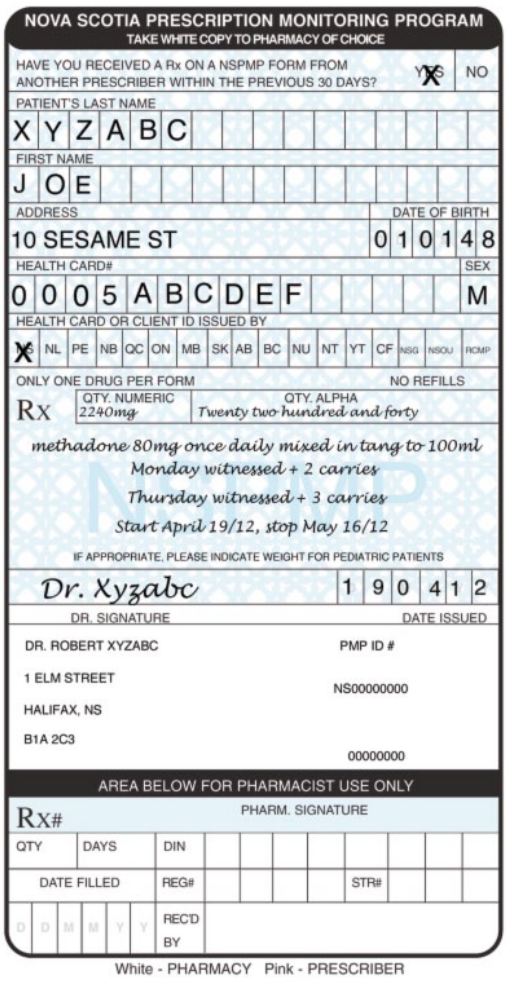
Rx# — PHARM. SIGNATURE

QTY | DAYS | DIN | DATE FILLED | REG# | STR# | D D M M Y Y | REC'D BY

White - PHARMACY Pink - PRESCRIBER

2. Prescription at a stable dose:

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



NOVA SCOTIA PRESCRIPTION MONITORING PROGRAM
TAKE WHITE COPY TO PHARMACY OF CHOICE

HAVE YOU RECEIVED A Rx ON A NSPMP FORM FROM ANOTHER PRESCRIBER WITHIN THE PREVIOUS 30 DAYS? YES X NO

PATIENT'S LAST NAME: XYZABC

FIRST NAME: JOE

ADDRESS: 10 SESAME ST

DATE OF BIRTH: 01 01 48

HEALTH CARD#: 0005ABCDEF

SEX: M

HEALTH CARD OR CLIENT ID ISSUED BY: X NL PE NB QC ON MB SK AB BC NU NT YT CF NSG NSOU RCMP

ONLY ONE DRUG PER FORM — NO REFILLS

Rx

QTY. NUMERIC: 2240mg

QTY. ALPHA: Twenty two hundred and forty

methadone 80mg once daily mixed in tang to 100ml
Monday witnessed + 2 carries
Thursday witnessed + 3 carries
Start April 19/12, stop May 16/12

IF APPROPRIATE, PLEASE INDICATE WEIGHT FOR PEDIATRIC PATIENTS

Dr. Xyzabc — DR. SIGNATURE

DATE ISSUED: 19 04 12

DR. ROBERT XYZABC
1 ELM STREET
HALIFAX, NS
B1A 2C3

PMP ID #: NS00000000

00000000

AREA BELOW FOR PHARMACIST USE ONLY

Rx# — PHARM. SIGNATURE

QTY | DAYS | DIN | DATE FILLED | REG# | STR# | D D M M Y Y | REC'D BY

White - PHARMACY Pink - PRESCRIBER

3. Prescription with take-home dosing:

This prescription represents a stable dose of methadone with twice 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 J: Patient Guide on Methadone Overdose

These are important things you need to know about methadone. If you don't understand these things, ask your methadone doctor or someone at the clinic.

You should always take the amount of methadone that the clinic gives 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.

You have to be extra careful about taking the amount of methadone the clinic gives you in the first two weeks, or you might 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 the clinic know right away. If you can't reach the 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.

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 the 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 the clinic know right away. If you can't reach the 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 from the clinic. 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: Sample Methadone Maintenance Clinical Note

Sample Methadone Maintenance Clinical Note		
Name: _____	**Psychological Issues Update:**	
Date: _____	Mood:	Normal – Other
	Sleep:	Normal – Insomnia
Current Methadone Dose: _____mg	Anxiety:	Absent – Present
Number of Take-home Doses: _____	Energy:	Normal – Other _____
Missed doses: Yes – No _____	Suicidal Ideation:	Absent – Present - NA
Supervised UDS:	**O/E**:	
Methadone: _____	Appearance:	Alert – Intoxicated
Cocaine: _____	Behaviour:	Normal – Abnormal
Opiates: _____	Gait:	Normal – Abnormal
Benzodiazepines: _____	Speech:	Normal – Abnormal
Oxycodone: _____	Eye contact:	Normal – Abnormal
Creatinine: Normal/Abnormal		
Interpretation of UDS_____	Reported methadone sedation:	Yes – No
Patient stated drug/alcohol use & route		
Since last visit:	Reported methadone withdrawal:	Yes – No
Opiates: Yes – No _____		
Cocaine: Yes – No _____	Take-home dose safety issues discussed:	Yes – No – N/A
Benzodiazepines: Yes – No _____		
Alcohol: Yes – No _____	Reviewed dangers of methadone diversion:	Yes – No – N/A
Other problematic drug use: Yes – No _____		
	Clinically stable:	Yes – No
Opioid Cravings:		
None – Mild – Moderate – Severe	Take-home doses locked up in a box:	Yes – No – N/A
Opioid Withdrawal:		
None – Mild – Moderate – Severe	Safe with take-home doses:	Yes – No

Sample Methadone Maintenance Clinical Note		
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 support:	Yes – No
Timing of Withdrawal from Last Dose: _____	Reported methadone withdrawal:	Yes – No
Counselling/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 L: 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.

Opioid	Metabolite
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.[187]

Drug	Detection time
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 (4 joints a week) 5 days Daily smoker 10 days Chronic smoker 4 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, tyramine, 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. The table below lists the range of cut-off values with tests currently being used in Nova Scotia. It is recommended that physicians consult with the laboratory to determine the specific cut-off values for the tests used.

	Cut-off Value
Amphetamine	300-1000 ng/ml
Benzodiazepine	150-300 ng/ml
Opioid	20-2000 ng/ml
THC	50-150 ng/ml
Barbiturates	200-300 ng/ml
TCA	300-1000 ng/ml
PCP	25 ng/ml
Cocaine	150-300 ng/ml
Methamphetamines	300-1000 ng/ml
Oxycodone	100 ng/ml
Methadone	100-300 ng/ml

Appendix M: 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 the clinic or pharmacy, they have to be very careful with it. People could get sick or die if you don't 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 don't understand these things, ask your doctor to explain them to you. If you still don't 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, they will be continued and you will be given more doses to take home once every four weeks.
8. The clinic 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 clinic staff can 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 the clinic know if your address or phone number changes.

Signatures

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

Appendix N: 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 counselling that has been helpful? Yes ❒ No ❒

11. Does your counsellor 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.[VI]

VI Adapted from "Tapering Readiness Inventory" from Treatment of Opiate Addiction with Methadone: A Counselor Manual, U.S. Department of Health and Human Services (DHHS) SMA94-2061. Reproduced in S. Brummett, R. Dumontet, L. Wermuth, M. Gold, J.L. Sorensen, S. Batki, R. Dennis & R. Heaphy (1986), Methadone Maintenance to Abstinence: The Tapering Network Project Manual, University of California, San Francisco. Methadone Maintenance: A Counsellor's Guide to Treatment, 242

Appendix O: Against Medical Advice (AMA)

Date:_____

I,_____ , acknowledge that _____ explained my condition to me and advised me of the potential risks and/or complications which could or would arise from refusal of medical care. I have also been advised that other unknown risks and/or complications are possible. Being aware that there are known and unknown potential risks and/or complications, it is still my desire to refuse the advised medical care.

I do hereby release _____ and_____(*clinic name*) from all liability resulting from any adverse medical condition(s) caused by my refusal of the recommended medical care.

Signature of Patient/Parent/Legal Guardian:

_____

Date_____

Witness _____

If witness acted as translator, check here _____

Name of translator_____

Appendix P: Form 2 – Medical Certificate for Involuntary Psychiatric Assessment (Part 1)

I, Dr. _____ (*full name*), a physician,
personally examined _____ (*full name of person*)
of _____ (*address of person*) on _____ /_____ /_____ (*dd/mm/yyyy*)
at _____ a.m./p.m. at _____ (*location of examination*).

It is my opinion that the person meets all of the following criteria (as set out in Sections 7 and 8 of the Act):

- The person apparently has a mental disorder
- The person, as a result of the mental disorder, (check one or both boxes)
  - ❒ Is threatening or attempting to cause serious harm to him/herself or has recently done so, has recently caused serious harm to him/herself
  - ❒ Is seriously harming or is threatening serious harm towards another person or has recently done so
  - ❒ The person is likely to suffer serious physical impairment or serious mental deterioration (or both)
- The person would benefit from psychiatric inpatient treatment in a psychiatric facility and is not suitable for inpatient admission as a voluntary patient

The following information supports my opinion that this person meets the criteria as checked above:

1. Observations from my examination of the patient:

_____

_____

_____

_____

2. Information from other sources:

_____

_____

_____

_____

Sources of above information (*identify specific sources*):

_____

_____

_____

I therefore certify that the person named in this certificate be detained, restrained and observed in _____ (*name of psychiatric facility*) for up to 72 hours for an involuntary psychiatric assessment by a psychiatrist.

_____ (Date of signature)

_____ (Signature of physician)

_____ a.m./p.m. (Time of signature)

_____ (Physician's name – printed)

Notes:

1. This certificate must be signed by the physician who examined the person, and, in accordance with Section 9 of the Act, is not effective unless signed within 72 hours of the examination.
2. A person cannot be taken into custody or detained unless this certificate is accompanied by one of the following:
   - A second Medical Certificate for Involuntary Psychiatric Assessment - Part 1 (Form 2) signed by another physician
   - A Medical Certificate for Involuntary Psychiatric Assessment - Part 2 (Form 3) signed by the same physician who signed Part 1.

Appendix Q: 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.**

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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 toursades 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 2-4 mg every 2 to 3 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 6 hours after naloxone or intubation is discontinued.

Departure AMA: If the physician feels the patient is not safe to leave, a Form 2 should be completed and the patient should be forced to stay.

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 R: 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 Obstuctive Pulmonary Disease

CPSBC - College of Physicians and Surgeons of British Columbia

CPSNS - College of Physicians and Surgeons of Nova Scotia

CPSO - College of Physicians and Surgeons of Ontario

CRNNS - College of Registered Nurses of Nova Scotia

CSC - Correctional Services of Canada

CWU - Chemical Withdrawal Unit

DMAC - District Medical Advisory Committee

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

MMT - Methadone Maintenance Treatment

NA - Narcotics Anonymous

NAS - Neonatal Absence Syndrome

NIHBI - Non-Insured Health Benefits (NS Pharmacare)

NPO - Nothing by Mouth

NSCP - Nova Scotia College of Pharmacists

OAT - Opioid Agonist Therapy

ODT - Opioid Dependence Treatment

PTSD - Post Traumatic Stress Disorder

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