Recommendations for the Medical Management of Substance Use Disorders in Withdrawal Management Services in Ontario

February 17, 2022

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Mentoring, Education, and Clinical Tools for Addiction: Partners in Health Integration (META:PHI)

Toronto

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Introduction

The purpose of these recommendations is to help clinicians working in WMS provide safe and effective medication assisted treatment. The recommendations complement the META:PHI publication entitled Withdrawal Management Services Manual. The manual contains clinical tools and protocols for Nurse Practitioners working in withdrawal management services in Ontario.

Withdrawal management services (WMS) are an essential part of the addiction care pathway. WMS provide shelter, monitoring, support, and referral to the ED when indicated. They also provide counselling and motivational interviewing and connect patients with community addiction, mental health, and social services. Some WMS offer day programs and medical treatment for withdrawal. Emergency departments, hospitals, police, and community agencies routinely send patients to WMS.

Medication-assisted treatment has been shown to reduce substance-related mortality, morbidity and health care utilization. Examples of medication-assisted treatment include opioid agonist treatment for Opioid Use Disorder and symptom-triggered benzodiazepine treatment for alcohol withdrawal. Unfortunately, many WMS lack the capacity to provide medication-assisted treatment. This can have severe consequences. Patients in untreated alcohol or opioid withdrawal are at high risk for relapse when they leave WMS, and a relapse reduces the likelihood that they will follow up with outpatient treatment. Relapse can also result in severe harm, including death from overdose.

Unfortunately, withdrawal management services do not always receive appropriate back up and support from emergency departments. Typically, when a person presents to a WMS setting in alcohol withdrawal, they are re-directed to the nearest emergency room for benzodiazepine treatment. Emergency departments frequently send patients home or back to WMS while still in active withdrawal, without providing loading doses for patients with a history of complicated withdrawal, or with a prescription for benzodiazepines but without a concrete plan for medication-assisted treatment. This contributes to high rates of patient drop-out and relapse and a general failure of the system to provide effective addiction care. Therefore it is critical that WMS have the capacity to provide medication-assisted treatment, without having to rely on emergency departments.

Several initiatives are underway to ensure that Ontario withdrawal management services are staffed by health care professionals. However, clinicians working in WMS face significant challenges in implementing medication-assisted treatment. They must deal with complex or difficult cases on their own, as they may be the only clinician on staff at the WMS. An additional challenge is that due to limited funding, healthcare staff are usually not available on site to oversee protocols that require monitoring over a number of hours, such as benzodiazepine loading or symptom-triggered benzodiazepine treatment of alcohol withdrawal. All of these issues reduce the capability of withdrawal management services to provide optimal care to people with substance use disorders.

Development of the WMS recommendations

These recommendations were written by a group of experienced addiction clinicians, and produced with the support of META:PHI (Mentoring, Education, and Clinical Tools for Addiction: Partners in Health Integration). The recommendations have undergone extensive peer review. The strength of the evidence supporting each recommendation is outlined in the narrative below the recommendation.

A. Recommendations for the medical management of Opioid Use Disorder (OUD) in Withdrawal Management Services

Recommendation 1. Withdrawal management services (WMS) must allow and encourage patients to continue Opioid Agonist Treatment (OAT) with methadone, buprenorphine or slow release oral morphine (SROM) during their stay at WMS. In most cases, buprenorphine, methadone or SROM should be dispensed daily under observation, either at the WMS facility or at a nearby pharmacy.

This recommendation is consistent with provincial and national standards. For example, the Health Quality Ontario Opioid Use Disorder Standard (1) states, "If a person receiving agonist therapy enters an inpatient facility (e.g., a hospital or residential addiction treatment program) or a correctional facility, their opioid agonist therapy should be continued without disruption" (p.24).

The three main opioid agonist medications, methadone, buprenorphine and SROM, are taken once daily under observation. These medications have a slow onset and long duration of action, so they do not cause euphoria or sedation when taken appropriately by patients who are tolerant to opioids. Opioid agonist medications provide substantial relief from withdrawal symptoms and cravings. Controlled trials and systematic reviews have shown that patients on OAT are at significantly lower risk of overdose death than those not on OAT (2, 3). OAT is associated with other positive outcomes, including marked reductions in drug-related crime and increases in employment rates (4). OAT prevents overdose in two ways: (a) most patients on OAT reduce the frequency and amount of their opioid use, and (b) patients on OAT become tolerant, or resistant, to the respiratory suppression caused by fentanyl and other potent opioids.

These protective effects are quickly lost if OAT is discontinued. Patients will usually relapse to opioid use because they cannot tolerate the withdrawal symptoms and cravings that accompany cessation of OAT. If individuals stop OAT while in WMS, withdrawal symptoms will often drive them to leave the program early, before they have a treatment plan in place. As well, without OAT, opioid tolerance is lost, putting these patients at high risk of overdose if they take "contraband" opioids during their WMS stay, or if they relapse to opioid use after leaving WMS.

OAT should be maintained even if the patient is being admitted to a residential program on discharge from the WMS. Patients remain at greater risk of overdose death if they are not on OAT, even if they attend a residential program (5-8).

Recommendation 2. Patients with OUD who are not on Opioid Agonist Treatment should be assessed by an OAT prescriber as soon as can be arranged after admission to WMS. The OAT prescriber would review the benefits and risks of OAT, and offer to initiate treatment. Sublingual buprenorphine/naloxone and long-acting injectable buprenorphine are considered first line treatments for opioid use disorders and are the safest option. Methadone and slow release oral morphine (SROM) are considered second and third line treatments respectively. SROM may also be added to methadone as adjunctive treatment when clinically indicated.

Buprenorphine is safer than methadone or SROM, because it is a partial opioid agonist that is unlikely to cause respiratory depression, in the absence of other sedating substances. For this reason, buprenorphine is the first line option, particularly for patients at higher risk for opioid toxicity, e.g., those who are older, have respiratory illness or who are on benzodiazepines. Buprenorphine is available in two formulations: Sublingual buprenorphine/naloxone, and long-acting injectable buprenorphine. The latter has a duration of action of 28-42 days, making it a useful option for patients who have difficulty attending the pharmacy daily.

Methadone is more effective at retaining patients in treatment (9), and is often the best option for patients who are at high risk for treatment drop out, for example, patients who inject fentanyl or heroin (10). Also, methadone is easier to initiate than buprenorphine when patients have been using opioids within the previous 1-2 days. Therefore, methadone might be considered over buprenorphine for patients who (a) have been unable to achieve a maintenance dose of buprenorphine because of precipitated withdrawal or other reasons; (b) have continued high risk opioid use despite being on a therapeutic dose of buprenorphine; (c) have had intolerable side effects with buprenorphine in the past, or (d) prefer methadone or SROM over buprenorphine. Also, buprenorphine induction may not be practical on evenings and weekends when there is limited staff coverage.

If a regulated health professional is on site, buprenorphine may be initiated using standard dosing protocols. The Clinical Opioid Withdrawal Scale (COWS) may be used to guide buprenorphine administration. If a regulated health care provider is not onsite, for example during the evening or weekend, then buprenorphine may be administered using “home induction” or “micro-induction” protocols. These protocols are intended for outpatient use and do not require onsite observation by a healthcare professional.

Recommendation 3. Once initiated, an OAT prescription should be continued for at least a week after discharge. WMS should facilitate an appointment with an OAT provider or clinic prior to the prescription end-date, or inform the patient about clinics that accept walk-in patients (for example, RAAM clinics and some community OAT clinics).

WMS must take steps to ensure continuity of OAT; patients who discontinue OAT are at high risk of relapse and overdose death. Ongoing community OAT can be provided by a Rapid Access Addiction Medicine (RAAM) clinic, community OAT clinic, other addiction clinic, or primary care clinic. When referred to a clinic that accepts patients by appointment, the WMS OAT prescriber should ensure that the patient has a firm appointment at the community OAT clinic prior to discharge. Whenever possible, the WMS prescriber should call the clinic or send a note so the receiving clinician has the necessary background clinical information on the patient. A “warm handover” can improve the chance of follow- through and optimizes care by the receiving clinician.

Recommendation 4. If the patient refuses even brief Opioid Agonist Treatment, then clonidine (along with symptomatic treatments) may be prescribed to treat symptoms of acute opioid withdrawal. On discharge, the patient should be connected to a RAAM clinic, community addiction clinic or primary care clinic.

Patients who decline OAT but accept clonidine should be advised that short-term clonidine treatment may help with withdrawal symptoms but is largely ineffective in preventing relapse. Opioid tolerance declines within days, putting patient at high risk for overdose if they relapse. Consider documenting the discussion, and having the patient sign a Loss of Tolerance form to support their understanding of their decision.
All patients who decline OAT should be given an appointment within a few days of discharge to a clinic where OAT can be commenced if they reconsider their decision; a RAAM clinic, community addiction clinic or a primary care clinic can all provide long term OAT. In many cases, RAAM clinics can facilitate and support primary care prescribing of OAT, particularly for buprenorphine.

Recommendation 5. Withdrawal management services should not undertake a rapid methadone or buprenorphine taper. Tapering should only be done by an OAT prescriber who is able to provide regular follow-up in the community.

Methadone and buprenorphine tapering should be undertaken slowly, over a period of many months, by an experienced OAT prescriber. Tapering off OAT is most likely to be successful if the patient has strong social supports and does not have an active psychiatric illness. An OAT prescriber can assess the patient's suitability for tapering and advise on a reasonable rate of dose tapering. Rapid tapering is associated with a marked increase in risk of relapse and overdose death (11), particularly in the first few weeks after cessation. One large study found that the risk of death increased six-fold in the first four weeks after discontinuing methadone treatment (2).

Sometimes patients in WMS express a strong desire to taper off methadone or buprenorphine, due to societal pressure or their own unrealistic expectations of the effectiveness of psychosocial treatment without OAT. The WMS clinician should attempt to maintain the patient's effective dose and refer them to a community OAT prescriber for on-going psychoeducation and evaluation. The culture and language of WMS staff should seek to destigmatize OAT and uphold the benefits and evidence behind it.

When a patient on OAT enters a residential treatment centre from WMS, the residential program should continue providing OAT for the duration of their admission, with a bridging script on discharge until the patient can connect with their regular OAT provider. If the centre is not able or willing to provide ongoing OAT, then WMS staff should assist the patient in finding an alternative treatment program.

Recommendation 6. Withdrawal management services should implement measures to reduce the risk of opioid overdose in patients with OUD, including take-home naloxone, counselling on overdose prevention, and connection with harm reduction services. This is particularly important in patients who have declined OAT.

- Patients with OUD should be given a take home naloxone kit and instructed in its use.
- Patients should be counselled on safe drug use strategies in the event of relapse. For example, "never

- use alone"; "carry naloxone"; "don't mix opioids with benzodiazepines or alcohol"; "use a 'test dose'."
- Patients who have discontinued their opioids while in WMS should be advised that they have lost their tolerance, and they could overdose if they relapse to their previous opioid dose.
- If the patient has discontinued an outpatient opioid prescription, the WMS clinician should send a note to the community prescriber to consider prescribing a lower dose should they decide to restart the opioid in the future (resuming a high dose after a period of abstinence could cause toxicity).
- Patients who use cocaine, crystal meth or illicitly manufactured opioid tablets should be warned that fentanyl is often added to these drugs without the user's knowledge, which could lead to unintended overdose and death. They should also be given a take-home naloxone kit with instructions on its use.
- Patients should be given contact information on harm reduction services, including the National Overdose Response Service, local supervised consumption services, and drug testing services.

Recommendation 7. Patients who are on moderate, therapeutic doses of a prescription opioid medication for chronic pain should be allowed to continue the same dose while in WMS.

Patients with substance use disorders who are on prescribed opioids for chronic pain are not necessarily addicted to them. Involuntary cessation of opioid medication can precipitate withdrawal, exacerbate pain, and cause depression and anxiety. Patients will quickly lose their opioid tolerance, putting them at high risk for overdose if they access potent opioids such as fentanyl or hydromorphone. Therefore, patients admitted to WMS for non-opioid substances should be allowed to remain on their opioid analgesic medication if they are on a moderate, stable dose and if they are not suspected of having an Opioid Use Disorder. As with other medications, prescription opioids will need to be stored and dispensed safely by staff on a daily basis according to the dosing schedule.

When possible, consultation with the opioid prescriber or review of pharmacy records may provide clarity. In general, higher doses of opioids are associated with a greater likelihood of OUD and a greater risk of death. Therefore clinicians should direct greater attention and inquiry to patients on opioid doses greater than 90 mg of morphine equivalents* per day (12).

*(morphine 15 mg = hydromorphone 3 mg = oxycodone 10 mg).

Recommendation 8. Patients on prescribed opioids should be offered Opioid Agonist Treatment if Opioid Use Disorder is suspected, or if the patient is having major opioid-related side effects.

The patient should be assessed for OUD if the doses are excessive for the underlying pain condition, if the doses are progressively increasing without a stabilizing benefit, or if there is evidence of significant misuse, e.g., 'snorting' or injecting oral tablets or buying opioids from the illicit drug market. The guidelines acknowledge that decisions in this regard can be difficult and that the reasons for continuing or discontinuing prescribed opioids should be thoroughly documented. WMS might consider implementing screening questionnaires (such as the COMM, ORT, PMQ or SOAPP-R tools) to aid in the identification of prescription OUD.

In most cases, buprenorphine is the first line medication for prescription opioid addiction. Methadone or SROM should be considered if the patient has failed buprenorphine in the past, if buprenorphine induction is

unsuccessful, or if the patient continues high risk opioid use despite being on an optimal dose of buprenorphine (see Recommendation 2).

OAT may also be offered to patients whose opioid medication may be causing or putting them at risk for harm, even if they do not necessarily have an opioid use disorder, for example: concurrent use of alcohol or sedating medications; COPD; or opioid-related side effects such as sleep apnea, fatigue or depression (13).

Recommendation 9. If there is an immediate safety concern arising from the patient's prescribed opioid dose while they are in WMS, the dose may be reduced, or the patient may be switched to a safer opioid such as buprenorphine.

The patient's opioid dose should be reduced if the patient is at imminent risk for opioid toxicity, because of their substance use, medical treatment for withdrawal, or their underlying medical condition. Consider a patient who is admitted to WMS for observation and management of alcohol withdrawal. The patient is being prescribed Hydromorph Contin 18 mg three times per day for chronic pain. This patient could be offered buprenorphine as a better chronic opioid option based on its safety profile and the risks to the individual with AUD. If the patient refuses to switch to buprenorphine, it would be prudent to substantially reduce the hydromorphone dose (for example, to 9 mg three times per day) while treating the alcohol withdrawal with carefully adjusted doses of a benzodiazepine.

Recommendation 10. Steps should be taken to avoid opioid toxicity when patients who are in a Safe Supply program are admitted to WMS.

Patients in "Safe Supply" (SS) programs are commonly prescribed hydromorphone tablets to reduce reliance on the toxic drug supply. Sometimes, SROM or methadone is co-prescribed along with hydromorphone. Before prescribing to the SS patient, the WMS clinician must confirm that a regulated health care professional (typically a pharmacist) has directly observed the patient taking all doses of hydromorphone and SROM for at least several days prior to WMS admission. This ensures that the patient will not experience opioid toxicity (sedation, overdose, falls, aspiration) if the patient takes the full dose while in WMS.
If the SS patient has been taking all opioid doses under observation by a pharmacist, then this dose may be continued while the patient is in WMS. If the patient is prescribed take-home hydromorphone tablets, then the following options should be considered:

1. The SS clinician may prescribe daily observed doses of oral hydromorphone +/- SROM for at least several days prior to admission to WMS. If the patient experiences no opioid toxicity, this would confirm that it is safe to continue the full dose during the patient's WMS stay.
2. Prior to attending WMS, the SS clinicians could convert the patient's hydromorphone dose to methadone, buprenorphine or SROM, dispensed under observation. If the client is already on OAT in combination with hydromorphone tablets, the OAT dose could be increased to compensate for discontinuation of hydromorphone. Alternatively, the WMS clinician could initiate OAT. After discharge from WMS, the SS clinician and the patient can resume SS if they choose.
3. Patients on injection OAT (iOAT) will need to be converted to oral OAT prior to admission. WMS does not have the capacity to supervise injections.
4. If the SS patient is unwilling to switch to methadone, buprenorphine or SROM, and is unwilling to take hydromorphone under observation at the pharmacy prior to attending WMS, then the WMS clinician

could prescribe SROM or a lower hydromorphone dose, e.g., one to two 8 mg tabs three times per day. This will reduce the risk of opioid-induced toxicity.

5. The hydromorphone or SROM dose may need to be reduced further, or withheld, if the patient receives additional sedating medications while in WMS, e.g. benzodiazepines for alcohol withdrawal management.
6. All opioid doses – hydromorphone, SROM, methadone and buprenorphine - should be taken orally and observed by WMS staff or at a nearby pharmacy. It is advisable to admit the patient when the WMS is optimally staffed, so that the patient's initial hydromorphone doses are observed e.g. earlier in the day. The SS clinician can later resume Safe Supply prescribing after discharge from WMS.

Recommendation 11. If the patient on prescribed opioids or OAT appears sedated, WMS staff should be instructed to transfer the patient to the ED.

All staff should be trained to recognize the signs of opioid toxicity and respond accordingly. Early signs can be subtle and easily missed; the patient may exhibit sweating, slowed speech, pinpoint pupils and 'nodding off', yet still remain able to respond to questions. These patients should be transferred to the ED as they may require supplemental oxygen, close observation and possibly naloxone treatment. They must not be left unattended as they can suffer respiratory arrest.

Recommendation 12. The community prescriber and pharmacist should be informed about changes to the patient's opioid prescription.

Patients who have had their opioid dose reduced or discontinued should be warned of the risks of resuming the previous opioid dose. The WMS clinician should also inform the community prescriber and the community pharmacy of any changes made to the patient's medication regimen. If the patient has been started on OAT, the community prescriber should be asked to discontinue the patient's previous opioid prescription.

Recommendation 13. Pregnant patients with OUD should be offered OAT as soon as possible.

Ideally, treatment of pregnant patients would be done in consultation with a provider experienced in both prenatal and obstetrical care and in addiction medicine, but we recognize that this is not always feasible..

Opioid Agonist Treatment during pregnancy is associated with marked improvements in both maternal and neonatal outcomes (14, 15). It should be offered immediately to patients with prescription or illicit opioid use disorder, as untreated opioid withdrawal carries a risk of miscarriage or premature delivery. Initiation of OAT in an inpatient setting is preferred whenever possible – e.g. WMS, hospital, or residential program. A therapeutic dose can be reached more quickly with inpatient initiation, making it more likely that the patient will remain in treatment. If inpatient initiation is not feasible, the OAT dose should be titrated as quickly as the outpatient titration protocol allows.

Buprenorphine-naloxone use during pregnancy has been shown to be safe, and is associated with milder Neonatal Abstinence Syndrome than methadone (16). For this reason, buprenorphine is generally considered

first line during pregnancy, particularly for patients who use prescription opioids. The patient should be switched to methadone if she continues high risk opioid use despite an optimal buprenorphine dose, or if induction onto buprenorphine is unsuccessful. Pregnant patients on methadone are more likely to remain in treatment than those on buprenorphine (16), and therefore methadone may be a better option for pregnant patients who are at high risk for treatment drop out, i.e. those who use potent opioids such as fentanyl or heroin, who are transiently housed, or those with concurrent mental illness.

If buprenorphine is used, the clinician should take steps to avoid precipitated withdrawal. If the patient is already in withdrawal when she presents to the WMS, then standard dosing protocols can be used. Otherwise, microdosing is the preferred method for avoiding precipitated withdrawal. Recent evidence suggests that buprenorphine can precipitate withdrawal in fentanyl users if given within 48 hours of the last use (17). Therefore, since there is currently little evidence on microdosing for fentanyl users, we would suggest that methadone be used as the first line for pregnant patients who use fentanyl.

SROM also appears to be safe in pregnancy and is a third line option. Patient preference based on informed decision-making should prevail.

B. Recommendations for the medical management of Alcohol Use Disorder (AUD) in WMS

Recommendation 14. Symptom-triggered benzodiazepine treatment should be offered to patients residing in WMS who are in moderate to severe alcohol withdrawal.

In symptom-triggered treatment, the severity of withdrawal is measured every 1-2 hours using a standardized scale such as the CIWA or SHOT (Sweating, Hallucinations, Orientation, Tremor) scale. While the CIWA scale has more evidence supporting its use, the SHOT takes less time to administer, and is based on objective signs (tremor, sweating) rather than subjective symptoms. Its scores have been shown to correlate closely with the CIWA scores (18). All staff can be trained in the appropriate use of these scales for monitoring purposes.

It is safest if symptom-triggered protocols are used by an onsite registered health care professional - RPN, RN, NP, PA or MD. When there is no health care professional on site, WMS staff will need to provide the medication on a schedule, as ordered by the prescriber - for example, “diazepam 10 mg every 4 hours for three doses, hold if drowsy”. Ideally, all WMS facilities would have 24/7 onsite nursing staff, making this constraining unnecessary.

Either diazepam 10-20 mg or lorazepam 1-4 mg is given if the patient scores above the cut off score (CIWA > or = 10; SHOT > or = 2). Diazepam is preferred in the absence of liver disease and significant medical co-morbidities, because of its long duration of action. Lorazepam is preferred in the elderly, those with liver or respiratory impairment, and in patients on methadone or other potent opioids (morphine, hydromorphone, oxycodone, transdermal fentanyl). Patients at very high risk for benzodiazepine toxicity may be given doses as low as 0.5-1 mg lorazepam.

Patients with a clear history of withdrawal seizures or DTs after cessation of alcohol can be treated with a loading dose of diazepam (20mg, Q1-2H for three doses), even if they do not yet display symptoms of withdrawal. There is evidence that early and aggressive benzodiazepine treatment prevents seizures and DTs.

Gabapentin may have a role either as a sole agent in mild alcohol withdrawal or as adjunctive treatment to

benzodiazepines in more severe alcohol withdrawal. Gabapentin is an effective anti- craving medication and doses can be maintained or adjusted after the acute withdrawal has resolved.

Recommendation 15. The WMS should have clear criteria for transferring the patient in alcohol withdrawal to the emergency department.

WMS staff will need training in these criteria, as the decision to transfer will need to be made by non-medical staff if there is no nurse, NP or MD available. Suggested criteria are listed below:

- High risk for benzodiazepine toxicity (e.g., liver failure, frail elderly, COPD, on methadone or high doses of opioids)
- Seizure or recent seizure history
- Worsening tremor despite several doses of diazepam or lorazepam
- Vomiting or profuse sweating, which could cause dehydration or electrolyte imbalances
- Concerning vital signs (irregular pulse, HR > 120, systolic BP ≥ 180, or diastolic BP ≥ 120
- Confusion, hallucinations or delusions, which could indicate the onset of withdrawal delirium
- Drowsiness or sleepiness out of keeping with the benzodiazepine dose. This could indicate a serious condition such as hepatic encephalopathy or Wernicke's encephalopathy (WE).
- Pregnancy

Recommendation 16. Alcohol withdrawal may be managed on an outpatient basis when it is safe to do so.

Alcohol withdrawal may be safely managed at home if the following conditions are met:

- The patient is in mild to moderate withdrawal and is not expected to require high loading doses of benzodiazepines (or they have already received a loading dose and their symptoms are now mild to moderate).
- The patient does not have a recent history of severe or complicated withdrawal, e.g., withdrawal seizures.
- The patient is 65 years of age or younger.
- The patient lives with someone who is reliable and can monitor their benzodiazepine and alcohol use.
- The patient is not on methadone or high opioid doses.
- The patient does not have cirrhosis with liver dysfunction.
- The patient does not have severe respiratory impairment, e.g., severe COPD.
- The patient does not have cognitive impairment or an active, severe psychiatric illness.

The patient should be given a prescription that will relieve moderate withdrawal symptoms but is unlikely to cause benzodiazepine toxicity – for example, diazepam 10 mg or lorazepam 2 mg q 4H PRN, maximum six doses in 24 hours, total of 12 tablets. The patient should be advised to only take the tablet for tremor; it is not intended for treatment of anxiety. The patient should also be advised to stop the benzodiazepine if they resume drinking, and to go to the ED if their symptoms worsen despite benzodiazepine treatment. Follow-up is recommended in the next 24-48 hours.

Recommendation 17. Anti-craving medications such as naltrexone, acamprosate and gabapentin should be routinely offered and prescribed onsite to all patients with AUD. The prescription should be continued until the patient can be seen by their primary care provider, or by a RAAM clinic or other addiction service.

Naltrexone and acamprosate are the first line anti-craving medications. Multiple controlled trials in observational studies have shown that these medications improve drinking outcomes and reduce ED visits and hospitalizations (19-24). Naltrexone reduces the reinforcing, euphoric effect of alcohol, while acamprosate relieves subacute withdrawal symptoms in patients who are abstinent. Naltrexone and acamprosate do not relieve acute withdrawal symptoms, but both medications can be prescribed while the patient is in WMS receiving treatment for withdrawal.

Gabapentin has also been shown to relieves mild acute withdrawal symptoms as well as subacute symptoms (25, 26), although the evidence of benefit is not as strong as for naltrexone and acamprosate. Gabapentin can be prescribed after treatment of acute withdrawal. Gabapentin can cause sedation, especially when combined with alcohol.

Recommendation 18. Thiamine should be routinely given to patients with Alcohol Use Disorder to prevent Wernicke's encephalopathy and Korkakoff syndrome.

Thiamine is used to prevent or treat Wernicke's encephalopathy for which AUD is a major risk factor. When resources allow, Thiamine 300mg IV/IM should be provided for 3-5 days. If parenteral thiamine is not an option, oral thiamine 300 mg per day should be given for the duration of the patient's stay at WMS. Since thiamine is not on the provincial formulary, hospital-based WMS should consider giving patients with AUD a one-month supply of thiamine 100 mg tablets when they are discharged (27-32).

Recommendation 19. Pregnant patients with AUD should be given priority access to addiction treatment.

A pregnant patient arriving at the WMS in alcohol withdrawal should be transported to the nearest hospital for monitoring and stabilization. Once stabilized in hospital, the patient may be cared for in the WMS. Ideally, care would be provided in n consultation with a provider with experience in prenatal care and addiction medicine, if available. Patients should be given priority access to outpatient and residential treatment programs.

Although they have not been extensively studied, naltrexone and acamprosate appear to be safe in pregnancy, and they may be prescribed in pregnant patients who are unable to maintain abstinence (33). Gabapentin use in late pregnancy has been associated with preterm labour and small for gestational age (34) so it should be used with caution. Disulfiram is contraindicated in pregnancy as it associated with fetal malformations.

C. Recommendations for Medical Management of Benzodiazepine Use and Benzodiazepine Use Disorder in WMS

Recommendation 20. Patients who are prescribed moderate, therapeutic doses of benzodiazepine medications for sleep or anxiety should be allowed to continue the same dose while in WMS, if the medication is not likely to cause the patient harm during their WMS stay.

Abrupt cessation of benzodiazepines is associated with a withdrawal syndrome characterized by anxiety, insomnia and poor concentration. While withdrawal from moderate doses is not dangerous, it can be intensely uncomfortable and may cause the patient to leave WMS and relapse.

If the patient is receiving benzodiazepines for the treatment of alcohol withdrawal, their standing prescription should be held, and resumed once withdrawal treatment is completed.

Recommendation 21. In patients residing at WMS, the prescribed benzodiazepine dose may be reduced if the dose puts that patient at imminent risk.

The patient's prescribed benzodiazepine dose should be reduced if the patient is at high risk for benzodiazepine toxicity while at WMS because of their substance use, initiation of new medications, or their underlying medical condition. The most common substances that increase risk of benzodiazepine toxicity are opioids and alcohol. For example, initiation of methadone treatment can be dangerous in patients on prescribed benzodiazepines. Medical conditions that increase the risk of benzodiazepine toxicity include COPD, pneumonia, and liver failure.

Generally speaking, benzodiazepine toxicity is more dangerous than benzodiazepine withdrawal. Benzodiazepine withdrawal develops gradually over days, and can be managed by dose adjustment, whereas toxicity can have immediate and severe consequences. To avoid toxicity, the prescribed benzodiazepine dose may need to be held, or reduced by 25-50% or more over several days or weeks, depending on the clinician's assessment of risk. The patient should be monitored carefully for sedation while in WMS and sent to the ED if there are any concerns.

Recommendation 22. Patients on prescribed benzodiazepines may be offered an outpatient taper if their current dose is causing side effects or putting them at risk for harm.

A trial of tapering may be indicated if the prescribed benzodiazepines are causing or putting the patient at risk for harm. For example:

- The patient may be having major side effects from their benzodiazepine, e.g., falls, fatigue, sedation, sleep apnea, or depression. Benzodiazepine-related harms are more common in the elderly.
- The patient is on an unsafe combination of medications, e.g., opioids and benzodiazepines.
- The patient is taking their prescription benzodiazepines in an unsafe manner, e.g., taking more than the prescribed dose, or taking the benzodiazepine while drinking heavily.

Tapering of prescription benzodiazepines can take several weeks or months. The patient's community prescriber should be informed of the taper and may assume responsibility for the taper when appropriate.

Recommendation 23. Patients with suspected Benzodiazepine Use Disorder should be offered a medically supervised benzodiazepine taper.

Illicit benzodiazepines are readily available on the street or through the internet. The treatment of choice is counselling, management of underlying psychiatric conditions, and gradual benzodiazepine tapering, often over many months.

Diazepam or clonazepam are the preferred tapering agents. Published protocols exist for outpatient tapering. It is worth noting that published tapering recommendations are generally based on benzodiazepine doses which are presumed to have been prescribed or verifiable. Clinicians should consider that illicit benzodiazepines may contain varied doses of different drugs and the reported dose of illicit benzodiazepines may not reflect the actual dose in diazepam equivalents taken by patients. By way of example, street Xanax is known to often consist of varied benzodiazepines and other illicit drugs. Clinical judgement and careful observation are required when switching a client from illicit benzodiazepines to prescribed benzodiazepines with the intent of tapering. Tapers may be started in patients who are residing in WMS, but if they are discharged after only a few days, an outpatient taper will be necessary. Daily dispensing is preferred. Patients on very high doses may benefit from an admission to a Medical Withdrawal Unit, if available.

Benzodiazepines should be given immediately if the patient is suspected to be in serious benzodiazepine withdrawal, e.g. delirium or psychosis. The dose should be titrated to effect, i.e. resolution of the withdrawal symptoms, and then slowly tapered. The patient should be transferred to the ED if the delirium or psychosis does not quickly resolve.

D. Recommendations for the Medical Management of Stimulant Use Disorders in WMS

Recommendation 24. There is no evidence yet to support the routine use of medications to treat stimulant withdrawal or stimulant use disorder. A medication trial may be considered if the patient is motivated to abstain but is experiencing strong cravings. Non-stimulant medications such as mirtazapine or topiramate are preferred.

Psychotherapeutic approaches have the strongest evidence of benefit for stimulant use disorder (35). Several medications have shown some evidence of benefit in controlled trials (36); however, the evidence should be viewed as preliminary. If a medication trial is undertaken, mirtazapine or topiramate should be considered first, as they have some evidence of benefit and safety (36-38).

Use of stimulants such as dexamphetamine and methylphenidate are not a recommended strategy to reduce illicit stimulant use in a WMS setting. In systematic reviews, psychostimulants were not associated with greater treatment retention; and they were associated with only short-term abstinence (2-3 weeks) (35, 39). Also, stimulants can themselves cause serious health problems, including psychological dependence, hypertension, cardiac arrhythmias, and infection if injected.

Patients without stimulant use disorder may continue taking prescription stimulants while in WMS if they are prescribed for adult ADHD or diagnosed narcolepsy. If the patient has both ADHD and a stimulant use disorder, consider using a non-stimulant medication such as atomoxetine; or if stimulants are used, consider extended-release formulations, with daily, every other day, or weekly pharmacy pick-ups.

Recommendation 25. Patients who report using crystal methamphetamine should be assessed for psychosis. Antipsychotic medications should be prescribed onsite when indicated. Clear criteria should be established for transferring psychotic patients to the emergency department.

Atypical antipsychotics improve psychotic symptoms such as hallucinations, disordered thoughts, and paranoia, and may improve treatment retention in patients with stimulant induced psychosis (36). Regular monitoring is important for the safety of all patients and staff. If the patient is relatively calm and not dysphoric, antipsychotic medications can be started in the WMS with close follow-up and urgent referral for psychiatric care. Transfer to the emergency department should be arranged if the patient is agitated or very anxious, acting in a potentially unsafe manner, or expressing thoughts of self- harm or harm to others. Police may need to be involved if there are safety issues or threatening behaviours.

E. Recommendations for the medical management of Cannabis Use Disorder in WMS

Recommendation 26. Patients with Cannabis Use Disorder may be offered medications to relieve withdrawal symptoms. The medication may be discontinued when the acute withdrawal has resolved, or maintained to relieve ongoing cravings (35).

Almost half of regular cannabis users experience withdrawal when they attempt to stop (40). The majority of acute cannabis withdrawal episodes are mild and resolve without the need for medical treatment. Cannabis withdrawal is characterized by insomnia, anxiety, fatigue, craving for cannabis, and physical symptoms which in some patients can be intensely uncomfortable (41). Controlled trials have found that nabiximols (Sativex®) and CBD oil relieve cannabis withdrawal symptoms and reduce cannabis use (42-47). The trials were short term (12 weeks), although one study found that the benefits of nabiximols persisted for up to three months after cessation (46). Both medications are expensive and not covered under ODB. Preliminary studies have also had positive results for nabilone, gabapentin and topiramate, and these medications are covered under ODB (42, 43). While the evidence for medical treatment of cannabis withdrawal is not robust, the medications are relatively safe, and they may be considered in clients with moderate to severe withdrawal symptoms, or in cases where patients have been unable to stop cannabis despite repeated attempts. The medication may be maintained after acute withdrawal has resolved if it is helping the patient reduce their cannabis use.

Screening for nicotine use should also occur, as these substances are often used concurrently, and nicotine use may increase with cessation of cannabis (48). Varenicline (Champix®) may help reduce cannabis use in patients who smoke both cannabis and tobacco. Nicotine Replacement Therapy (NRT) should be discussed with all clients.

Recommendation 27. Clients should not be permitted to smoke cannabis on WMS property.

Cannabis may be used orally, and vaping may be allowed per site policy. Smoking should not be permitted on site, even if the cannabis is prescribed.. Smoking exposes other clients to second-hand smoke. The WMS clinician should not assume that a patient's cannabis use is safe or therapeutic if it has been prescribed by a medical cannabis clinic; these clinics commonly prescribe high doses of cannabis with high concentrations of THC, for conditions for which cannabis is not indicated or is contraindicated (49). Regular use of THC is associated with cannabis use disorder, anxiety and mood disorders, psychosis, and poor psychosocial functioning.

F. Recommendations for medical management of Nicotine Use Disorder in WMS

Recommendation 28. WMS patients who smoke cigarettes should be routinely offered NRT, bupropion or varenicline.

The risks of nicotine consumption should be reviewed, and all patients should be offered NRT. Smokers who are in the "action" phase of change should be offered bupropion or varenicline if NRT is ineffective. E-cigarettes/vaping may be allowed per site policy; there is evidence that vaping nicotine is as, or more, effective than NRT (50). Smoking on site should be discouraged, but may be permitted in designated outside areas, as per individual WMS policy.

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