Safe prescribing practices for addictive medications and management of substance use disorders in primary care: A pocket reference for primary care providers

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META:PHI

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Acknowledgments

Mentoring, Education, and Clinical Tools for Addiction: Primary Care–Hospital Integration (META:PHI) is an ongoing initiative to improve the experience of addiction care for both patients and providers. The purpose of this initiative is to set up and implement care pathways for addiction, foster mentoring relationships between addiction physicians and other health care providers, and create and disseminate educational materials for addiction care. This handbook is intended as a quick-reference tool for primary care providers to assist them in implementing best practices for prescribing potentially addictive medications and managing substance use disorders in primary care.

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META:PHI

Part I: Working with patients

Introduction

A strong therapeutic alliance is integral to helping patients recover from a substance use disorder. Talking to patients about their substance use can be challenging for clinicians. This section briefly outlines some general guidelines for working with patients with substance use disorders and some therapeutic techniques that have been shown to be useful in treating patients; clinicians are encouraged to incorporate these techniques when treating patients for addiction.

General guidelines

- Be aware of patients' possible guilt/shame about addiction.
  - Reframe addiction as **biomedical problem** ("You have a substance use disorder") rather than **moral failing** ("You are an addict").
  - Be **non-judgmental** in your approach.
- Encourage patient to take responsibility for getting help for addiction **without blame**.
- Understand difficult patient behaviours as manifestations of illness.
  - Patients with substance use disorders tend to be disorganized, late for appointments, miss appointments, request urgent appointments, etc.
  - Substance use disorders make patients' lives much more difficult to control.

- Use **brief intervention** techniques to engage patient in treatment (1):
    1. Give feedback from assessment.
    2. Inform patient about health risks and offer help.
    3. Assess patient's readiness to change.
    4. Negotiate strategies for change.
    5. Arrange follow-up.
- Refer patients to psychosocial treatment when indicated.
    - Many options for patients to choose from: residential vs. outpatient, individual vs. group, religious vs. secular, etc.
    - Effective psychosocial treatment models for patients with substance use disorders include Seeking Safety (2), structured relapse prevention (3), and cognitive behavioural therapy (4, 5).

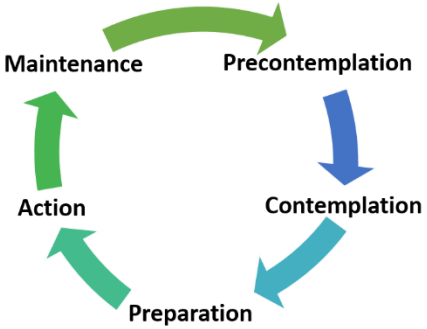
Encouraging behavioural change

When talking to patients about problematic substance use, the role of the care provider is to inform patients of their options and express willingness to help in order to enhance the patient's motivation. The approach taken for each individual patient depends on the patient's current stage of change.

Stages of change

The transtheoretical model of behaviour change (6) recognizes five stages of change:

1. Precontemplation
    - Not ready to change pattern of substance use.
    - May be unaware that their substance use is problematic.
2. Contemplation
    - Becoming aware that substance use is problematic.
    - Beginning to see some advantages to change.
    - Considering making a change in the next six months.
3. Preparation
    - Commitment to change.
    - Planning, decision-making, goal-setting.
4. Action
    - Change in progress.
    - Encountering consequences of changing substance use, both positive (e.g., more energy, improved relationships) and negative (e.g., withdrawal, boredom).
    - Establishing new habits and new lifestyle.
5. Maintenance
    - Work to sustain new habits.
    - Learn to deal with challenges and setbacks.



Enhancing motivation

The Center for Substance Abuse Treatment recommends using different strategies to enhance motivation depending on the patient's stage of change (7):

Pre-contemplation	Work to establish **trusting relationship** Open the door to conversations about substance use • Present facts • Express concern • Ask how patient sees their substance use • Offer help without pressure
Contemplation	Acknowledge **difficulty** of change Normalize **ambivalence** Explore patient's reasons **for** and **against** making a change Explore patient's **values** and **strengths** Emphasize patient's free choice Reiterate **help** and **support**
Preparation	Work together to create a **concrete plan** • What is the goal? • What are the strategies/tools (e.g., medication, counselling)? • What is the timeline? • What supports will patient use? • How will patient address barriers/setbacks?
Action	See patient frequently to check in and support engagement Acknowledge **successes** and address **setbacks** Support change through **small steps**
Maintenance	Acknowledge **success** Support healthy lifestyle changes Maintain **contact**

Trauma-informed care

Trauma occurs when an individual is in a frightening situation that overwhelms their ability to cope. As a result, the individual is left with feelings of fear, horror, and helplessness that can last for the rest of their life. Many patients with a substance use disorder have a trauma history; care providers should this in mind in their interactions with patients.

Roots and effect of trauma

- Adverse childhood events (8):
  - Strong correlation between adverse childhood events (ACEs) and development of risk factors for disease, including substance use disorders.
  - Risk increases with number of ACEs.
- Multigenerational trauma: Trauma experienced by parents affects children.
  - E.g., children of Holocaust survivors, children of survivors of Canadian residential school system.
  - Effect on individuals, families, and communities.
- Trauma can have a profound effect on people's lives:
  - Loss of stability
  - Abnormal neurodevelopment
  - Mental health problems (e.g., PTSD)
  - Substance use as a **coping mechanism**

Principles of trauma-informed care

Acknowledgment	Listen, empathize, normalize, validate.
Trust	Be honest about your knowledge, skills, and limitations as a care provider. Provide **transparency** and **shared power** in decision making. Enforce consistent **boundaries**.
Collaboration	Emphasize patient's **choice** and **control**
Compassion	Not "What's wrong with you?" but "What happened to you?" Identify the patient's needs and explore implications for care.
Strength-based	Acknowledge **resilience**. Acknowledge that coping mechanisms (e.g., substance use) are **understandable** and **logical**.
Safety	Physical safety: Well-lit office, safe building, comfortable environment. Emotional safety: Avoid re-traumatizing patient.

Asking about trauma

- Spend some time developing initial rapport before asking about trauma.
- Be prepared to define trauma:
  - "Sometimes we see or experience things that are very violent, frightening, or overwhelming, and those things can stay with us for many years if we don't get help dealing with them. There is lots of research to show that experiences like these can have an impact on our physical and mental health."
- Explain link between trauma and substance use:
  - "Memories of traumatic experiences can cause a lot of overwhelming emotions, and a lot of people use drugs or alcohol as a way to cope with those emotions."

- Ask about trauma in a **non-judgmental** way:
  - "Have you ever experienced any difficult life events, either in childhood or as an adult, that you think might be related to some of the things you are struggling with now?"
- Ask without pressure:
  - "Is that something you would feel comfortable talking to me about?"
  - "I know it can be really difficult to talk about these things. You don't have to tell me about it, but just remember that you can, if you think it might be helpful."
- Responding to disclosure:
  - Acknowledge **disclosure**: "I appreciate you sharing this with me. I know it's not easy to do."
  - Acknowledge **impact**: "That sounds like a really difficult experience. It must have been really hard for you."
  - Express **compassion**: "What happened wasn't your fault." "Nobody deserves to be treated that way." "I'm so sorry that happened to you."
  - **Normalize** reactions: "It makes a lot of sense that you would have difficulty trusting people after that; you're trying to protect yourself." "I can understand how drinking keeps you from having to think about such a frightening memory."

Assessing effect of trauma

- Who has patient disclosed to?
- Is patient experiencing ongoing effects (e.g., anxiety, flashbacks)?
- Is patient using harmful coping strategies (e.g., substance use, self-harm)?

- Has patient had any therapy in regards to their trauma?
- If trauma is unresolved, refer patient to specialized treatment:
  - Trauma-focused cognitive behavioural therapy (TF-CBT)
  - Eye movement desensitization and reprocessing (EMDR)
  - Seeking Safety
  - Dialectical behavioural therapy (DBT)
- Publicly funded programs often have long waiting lists; offer patient ongoing support while they are awaiting treatment.

Part II: Alcohol

Introduction

Until recently, primary care providers' role has been restricted to treating medical complications of alcohol misuse and referring patients for specialized alcohol treatment. However, primary care is an ideal setting for the long-term management of alcohol disorders. Primary care practitioners can provide ongoing advice (9); there is evidence that the length of treatment has a greater impact on outcome than the intensity of treatment (10). Surveys suggest that patients would much prefer to receive treatment in a primary care setting than in a formal addiction setting. Addiction treatment in a primary care setting also enables the provision of ongoing medical care to the addicted patient. Controlled trials, cohort studies, and a systematic review have demonstrated that patients with a substance-related medical condition had reductions in hospitalizations, emergency room visits, health care costs, and possibly mortality if their primary care practitioner had addiction medicine training, or if addiction treatment was integrated with primary care (11-14). However, despite compelling evidence for primary care provider involvement with alcohol use disorders, clinicians do not consistently screen for alcohol or drug problems, counsel their addicted patients, or refer patients to formal treatment (15). A strong and growing body of evidence indicates that these interventions are effective, easily learned, and practical in a primary care setting. What follows is a brief overview of these interventions.

Diagnostic continuum of alcohol problems

Alcohol use occurs along a spectrum of severity: abstinence, low-risk drinking, at-risk drinking, and alcohol use disorder (AUD).

Low-risk drinking

The Canadian Centre for Substance Abuse released these low-risk drinking guidelines in 2010 (16):

Note: These guidelines are not intended to encourage people who choose to abstain for cultural, spiritual or other reasons to drink, nor are they intended to encourage people to commence drinking to achieve health benefits. People of low bodyweight or who are not accustomed to alcohol are advised to consume below these maximum limits.

Guideline 1

Do not drink in these situations:

- When operating any kind of vehicle, tools, or machinery
- Using medications or other drugs that interact with alcohol
- Engaging in sports or other potentially dangerous physical activities
- Working
- Making important decisions
- If pregnant or planning to be pregnant
- Before breastfeeding
- While responsible for the care or supervision of others
- If suffering from serious physical illness, mental illness, or alcohol dependence

Guideline 2

If you drink, reduce *long-term* health risks by staying within these average levels:

Women: 0-2 standard drinks* per day, no more than 10 standard drinks per week

Men: 0-3 standard drinks* per day, no more than 15 standard drinks per week

Always have some non-drinking days per week to minimize tolerance and habit formation. Do not increase drinking to the upper limits as health benefits are greatest at up to one drink per day. Do not exceed the daily limits specified in Guideline 3.

Guideline 3

If you drink, reduce *short-term* risks by choosing safe situations and restricting your alcohol intake:

- Risk of injury increases with each additional drink in many situations. For both health and safety reasons, it is important not to drink more than three standard drinks* in one day for a woman and four standard drinks* in one day for a man.
- Drinking at these upper levels should only happen *occasionally* and always be consistent with the *weekly* limits specified in Guideline 2. It is especially important on these occasions to drink with meals and not on an empty stomach; to have no more than two standard drinks* in any three-hour period; to alternate with caffeine-free, non-alcoholic drinks; and to avoid risky situations and activities. Individuals with reduced tolerance, whether due to low bodyweight, being under the age of 25 or over 65 years old, are advised to never exceed Guideline 2 upper levels.

Guideline 4

When pregnant or planning to be pregnant:

The safest option during pregnancy or when planning to become pregnant is to not drink alcohol at all. Alcohol in the mother's bloodstream can harm the developing fetus. While the risk from light consumption during pregnancy appears very low, there is no threshold of alcohol use in pregnancy that has been definitively proven to be safe.

Guideline 5

Alcohol and young people:

Uptake of drinking by youth should be delayed at least until the late teens and be consistent with local legal drinking age laws. Once a decision to start drinking is made, drinking should occur in a safe environment, under parental guidance and at low levels (i.e., one or two standard drinks* once or twice per week). From legal drinking age to 24 years, it is recommended women never exceed two drinks per day and men never exceed three drinks in one day.

*A **standard drink** is defined as a 341 ml (12 oz.) bottle of 5% strength beer, cider, or cooler; a 142 ml (5 oz.) glass of 12% strength wine; or a 43 ml (1.5 oz.) shot of 40% strength spirits.

At-risk drinking

At-risk drinkers have the following properties:

(a) Patient drinks above recommended guidelines.

(b) Patient may have alcohol-related problems.

- Psychological problems: insomnia, anxiety, depression
- Social problems: spending inadequate time with family, reduced work performance, impaired driving charges
- Physical problems: gastritis, hypertension, fatty liver, recurrent trauma, sexual dysfunction

(c) Patient does not meet the DSM-V criteria for an alcohol use disorder.

Alcohol use disorder (AUD)

The DSM-V gives the following criteria for an AUD (17):

(a) Alcohol taken in larger amounts or over a longer period of time than intended.
(b) Repeated unsuccessful efforts to reduce use.
(c) Great deal of time spent obtaining or using alcohol, or recovering from its effects.
(d) Strong cravings or urges to drink.
(e) Recurrent use resulting in a failure to fulfill major responsibilities.
(f) Continued use despite alcohol-related social or interpersonal problems.
(g) Reduction of major activities because of alcohol (e.g., missing work, spending less time with children or spouse).
(h) Repeatedly drinking in situations or activities where intoxication is dangerous.
(i) Continued use despite knowledge of alcohol-related physical or psychological problems.
(j) Tolerance (need to drink more to achieve the same effect, or diminished effects with continued use of the same amount of alcohol).
(k) Withdrawal (e.g., tremors, sweating and/or anxiety in morning or afternoon, relieved by drinking; withdrawal seizures).

Patients who meet two or three of these criteria have a **mild** AUD, four to five criteria indicate a **moderate** AUD, and six or more indicate a **severe** AUD.

Screening and identification

Alcohol consumption history

- Ask all adolescent and adult patients at baseline and annual physical.
- Elicit a specific weekly consumption.
- Convert responses into standard drinks: 12 oz. of beer, 5 oz. of wine, or 1.5 oz. of spirits.
- Ask about patients' maximum consumption on one day in the past one to three months.

Common errors in alcohol history

- Not asking.
- Accepting vague answers (e.g., "I just drink socially").
- Not converting to standard drinks (most people pour large drinks at home).
- Missing binge consumption (many patients do not mention periodic heavy consumption when asked about "average" or "typical" drinking).

Screening questionnaires

- Three common surveys: CAGE (18-20), binge drinking question (21), AUDIT (22).
- Best as waiting room questionnaire, but can be incorporated into clinical interview.
- Sensitivity for detecting alcohol problems in primary care 70–80%.
- Positive screens require further assessment.

(1) CAGE questionnaire

Have you ever felt you ought to **C**UT DOWN on your drinking? Have people **A**NNOYED you by criticizing your drinking? Have you ever felt bad or **G**UILTY about your drinking? Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover (**E**YE-OPENER)?

* A positive screen is 2/4 for men, 1/4 for women.

* CAGE is retrospective; it may indicate a past problem rather than a current one.

(2) Binge-drinking question

How many times in the past year have you had five (men) / four (women) or more drinks in one day?

* Once or more is a positive screen.

(3) Alcohol use disorders identification test (AUDIT)

1. How often do you have a drink containing alcohol?				
0 Never	**1** Monthly or less	**2** 2–4 times per month	**3** 2–3 times per week	**4** 4+ times per week
2. How many drinks containing alcohol do you have on a typical day when you are drinking?				
0 1–2	**1** 3–4	**2** 5–6	**3** 7–9	**4** 10+
3. How often do you have 6 or more drinks on one occasion?				
0 Never	**1** Less than monthly	**2** Monthly	**3** Weekly	**4** Daily or almost daily
4. How often during the last year have you found that you were not able to stop drinking once you had started?				
0 Never	**1** Less than monthly	**2** Monthly	**3** Weekly	**4** Daily or almost daily
5. How often during the last year have you failed to do what was expected of you because of drinking?				
0 Never	**1** Less than monthly	**2** Monthly	**3** Weekly	**4** Daily or almost daily
6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?				
0 Never	**1** Less than monthly	**2** Monthly	**3** Weekly	**4** Daily or almost daily
7. How often during the last year have you had a feeling of guilt/remorse after drinking?				
0 Never	**1** Less than monthly	**2** Monthly	**3** Weekly	**4** Daily or almost daily
8. How often during the last year have you been unable to remember what happened the night before because you had been drinking?				
0 Never	**1** Less than monthly	**2** Monthly	**3** Weekly	**4** Daily or almost daily
9. Have you or someone else been injured because of your drinking?				
0 No	**2** Yes, but not in the past year		**4** Within the past year	
10. Has a relative, friend, doctor, or other health worker been concerned about your drinking or suggested that you cut down?				
0 No	**2** Yes, but not in the past year		**4** Within the past year	

* A score of 8+ suggests at-risk drinking or a mild AUD.

* The higher the score, the greater the likelihood of AUD. A score of 20+ indicates a strong chance of AUD.

Laboratory measures

Laboratory measures can be used to confirm clinical suspicion and monitor response to treatment (23, 24).

GGT	• 35–50% sensitive for detecting 4+ drinks/day • Half-life four weeks • Also elevated by hepatic enzyme inducers (e.g., phenytoin), diabetes, obesity, etc.
MCV	• Somewhat less sensitive than GGT • At least three months to return to baseline • Also elevated by medications, folic acid and B12 deficiency, liver disease, hypothyroidism, etc.

Identification of alcohol problems in primary care

System	Presenting complaint	Clue that problem may be alcohol-related
Musculo-skeletal	Trauma	• Recurrent • Not related to sports activities • Occurs during/after social event
GI	Gastritis and esophagitis	• Resolved with abstinence or reduced drinking • Not triggered by usual risk factors (fatty meals, NSAIDs)
Hepatic	Fatty liver Elevated GGT/AST Signs of liver dysfunction	• Not explained by other conditions (obesity, diabetes, viral hepatitis, medication use)
Cardio-vascular	Hypertension	• 3+ standard drinks consumed daily • Relatively resistant to anti-hypertensive meds • BP improves with abstinence or reduced drinking

System	Presenting complaint	Clue that problem may be alcohol-related
Sleep	Sleep apnea Insomnia	• Resolves with abstinence or reduced drinking • No trouble falling asleep but disturbed by vivid dreams in middle of night and/or early morning
Social	Problems with relationships at home and at work	• Fails to meet work or family obligations because of drinking or recovering from drinking • Is argumentative, emotionally labile, or sleepy after 4+ standard drinks
Psychiatric	Anxiety and depression	• Rapid improvement in anxiety or mood with first 1–3 drinks (though mood often worsens with 4+ standard drinks) • Worse during periods of drinking, better with reduced drinking/abstinence • Relatively unresponsive to medical or counselling interventions to improve anxiety/mood

Diagnosis: At-risk drinking, mild AUD, moderate AUD, severe AUD

Most heavy drinkers are **at-risk drinkers** or have a **mild AUD**. They drink above the low-risk guidelines, but are often able to drink moderately, have not suffered serious social consequences of drinking, and do not go through withdrawal. They often respond to brief advice and reduced drinking strategies.

Patients with **moderate to severe AUDs** often have withdrawal symptoms, rarely drink moderately, continue to drink despite knowledge of social or physical harm, and spend a great deal of time drinking, neglecting other responsibilities. They generally require abstinence and more intensive treatment.

	At-risk drinking or mild AUD	Moderate or severe AUD
Withdrawal symptoms	No	Often
Standard drinks	14+ per week	40–60+ per week
Drinking pattern	Variable; depends on situation	Tends to drink a set amount
Daily drinker	Less likely	More likely
Social consequences	None or mild	Often severe
Physical consequences	None or mild	Often severe
Socially stable	Usually	Often not
Neglect of major responsibilities	No	Yes

Management of at-risk drinking and mild AUDs

Patient intervention (25, 26)

- Review low-risk drinking guidelines.
- Link alcohol to patient's own health condition if possible.
- Review non-specific sedative effects of alcohol (fatigue, insomnia, low mood).
- Ask patient to commit to a drinking goal: reduced drinking or abstinence.
- If unwilling to commit, continue to ask about drinking at every office visit.
- If reduced drinking goal chosen:
  - Have patient specify when, where and how much they intend to drink.
  - Give tips on avoiding intoxication (see below).
  - Ask patient to keep a daily record of drinking.

- Monitor GGT and MCV at baseline and follow-up.
- Identify triggers to drinking (e.g., emotions, social events) and develop plan to deal with triggers.
- Have regular follow-ups.
- Consider referral to alcohol treatment program if problem persists.

Tips to reduce alcohol intake

- Set a goal for reduced drinking. The goal should specify the amount and circumstances of each drinking day (e.g., no more than three standard drinks on Thurs, Fri, Sat; no drinking alone). The goal should include non-drinking days.
- Record drinks on a calendar, log book, or app.
- Arrive and leave drinking events at a pre-determined time (e.g., only stay at a pub or party for three hours). If this is unlikely to work, avoid drinking events altogether.
- Avoid people and places associated with heavy drinking.
- Eat before and while drinking.
- Start drinking later in the evening or night.
- Switch to a less preferred alcoholic drink.
- Pace your drinking (e.g., no more than one drink per 45–60 minutes).
- Sip drinks slowly.
- Alternate alcoholic drinks with non-alcoholic drinks.
- Dilute drinks with mixer.
- Wait for 20 minutes between deciding to drink and actually having a drink.

Management of moderate and severe AUDs

Patient intervention

- Explain health effects of alcohol, linking them to patient's condition; reversible with abstinence.
- Explain that within days or weeks of abstinence, most patients have improved sleep, mood, and energy level.
- Explain that alcohol use disorder is a chronic illness, that it can happen to "good" people, that effective treatments are available, and that prognosis is good with treatment.
- Ask whether patient is willing to commit to a drinking goal (abstinence or reduced drinking).
- If the patient is not ready to commit, ask about drinking and readiness to change at each visit.
- If ready to commit, negotiate a written drinking goal:
  - Abstinence is more likely to be successful.
  - If reduced drinking goal is chosen, encourage a time-limited trial.
- Consider planned detoxification if at risk for withdrawal (6+ standard drinks/day, morning or afternoon tremor/anxiety).
- Treat concurrent conditions (e.g., anxiety, depression, hypertension, liver disease).
- Routinely offer pharmacotherapy: disulfiram, naltrexone, acamprosate, baclofen, gabapentin, topiramate.
- Encourage patient to make healthy lifestyle choices:
  - Avoid people and places associated with drinking.
  - Spend time with supportive family and friends.
  - Take daily walks (if health permits).
  - Maintain regular sleeping/waking schedule.
  - Plan regular activities outside the house as feasible.

- Review options for formal treatment (residential, day, outpatient).
- Encourage access to local addiction services through a local directory.
- Recommend AA for group support, practical advice, and as a way to overcome loneliness and boredom; suggest Al-Anon for families or caregivers (27).
- Arrange follow-up; routinely monitor drinking through self-report, GGT, MCV.
- Acknowledge successes, even if partial or temporary.
- If patient relapses, encourage contact and reconnection with treatment.

Management of alcohol withdrawal

Clinical features of withdrawal

- Starts 6–12 hours after last drink
- Peaks at 24–72 hours
- Resolves in 3–10 days (or longer)
- Tremor is most reliable feature (postural, intention, not a resting tremor)
- Other features: sweating, vomiting, anxiety, tachycardia, hypertension, ataxic gait

Risk factors for withdrawal

- 6+ standard drinks/day for 1+ weeks; risk increases with amount consumed
- Past seizures/DTs risk factor for future seizures/DTs

Withdrawal management options

Indications for office management of withdrawal:

- Reports frequent withdrawal symptoms
- Committed to abstinence and willing to start psychosocial treatment and/or anti-alcohol medications
- No history of seizures, DTs, or ED visits or hospitalizations due to withdrawal
- Not on high doses of opioids or sedating medications.
- Does not have cirrhosis with liver dysfunction
- Has supports at home

Indications for home management of withdrawal:

- Office management not feasible
- A spouse, relative, or friend agrees to dispense the medication
- No history of severe withdrawal (seizures, delirium, hospital admissions)
- Treatment plan in place (anti-alcohol medication, ongoing counselling, AA, etc.)
- Age < 65
- No hepatic decompensation (ascites, encephalopathy)
- Patient agrees not to drink while taking medication

Indications for ED management of withdrawal:

- History of seizures, DTs, or ED visits or hospitalizations due to withdrawal
- On high doses of opioids or sedating medications
- Has advanced cirrhosis
- Lacks supports at home
- No treatment plan in place
- Age ≥ 65

Office withdrawal protocol

Before treatment:

- Advise patient to have their last drink the night before the morning appointment.
- If patient shows up intoxicated, reschedule and/or admit to withdrawal management.

Withdrawal severity scales:

(1) Clinical Institute Withdrawal Assessment for Alcohol, Revised (CIWA-Ar) (28): Standard monitoring scale, strong evidence of validity

(2) Sweating, Hallucination, Orientation, Tremor (SHOT) scale (29): Simple scale validated in the ED

Diazepam vs. lorazepam:

- Diazepam is first-line medication.
- Use lorazepam instead if patient is 60 or older, is on opioids or other sedating medications, has low serum albumin from any cause, or has liver dysfunction (i.e., clinical or laboratory signs of cirrhosis, e.g., low albumin, high bilirubin/INR).

Treatment:

- Administer CIWA-Ar or SHOT every 1–2 hours.
- Give diazepam 10–20 mg (PO/IV) or lorazepam 2–4 mg (SL/PO/IM/IV) for CIWA-Ar ≥ 10 or SHOT ≥ 2.
- Treatment is complete when CIWA-Ar < 8 or SHOT ≤ 1 on 2 consecutive occasion and patient has minimal or no tremor.
- Send the patient to ED if patient has not improved or has worsened despite 3–4 doses; if they display marked tremor, vomiting, sweating, agitation, or confusion; or if they have risk factors for electrolyte imbalance or arrhythmias (e.g., diuretics, heart disease, diabetes).

On discharge:

- Initiate anti-alcohol medication.
- Advise patient to attend AA or other psychosocial treatment program.
- Arrange follow-up in a few days (1–2 days if lorazepam was used).
- Ensure patient leaves accompanied by friend or relative.
- If uncertain whether withdrawal is resolved, give diazepam 10 mg q4h (4–5 10 mg tablets) or lorazepam 1–2 mg q4H (10–12 1 mg tablets) for tremor, to be dispensed by partner if possible.

(1) CIWA-Ar scale

TREMOR Arms extended and fingers spread apart Observation 0 no tremor 1 not visible, but can be felt fingertip to fingertip 2 3 4 moderate, with patient's arms extended 5 6 7 severe, even with arms not extended	**NAUSEA AND VOMITING** Ask "Do you feel sick to your stomach? Have you vomited?" Observation 0 no nausea and no vomiting 1 2 3 4 intermittent nausea with dry heaves 5 6 7 constant nausea, frequent dry heaves and vomiting
TACTILE DISTURBANCES Ask "Have you any itching, pins and needles sensations, any burning or numbness, or do you feel bugs crawling on your skin?" Observation 0 none 1 very mild itching, pins and needles, burning or numbness 2 mild itching, pins and needles, burning or numbness 3 moderate itching, pins and needles, burning or numbness 4 moderately severe hallucinations 5 severe hallucinations 6 extremely severe hallucinations 7 continuous hallucinations	**AGITATION** Observation 0 normal activity 1 somewhat more than normal activity 2 3 4 moderately fidgety and restless 5 6 7 paces back and forth during most of the interview, or constantly thrashes about

HEADACHE, FULLNESS IN HEAD Ask "Does your head feel different? Does it feel like there is a band around your head?" Do not rate for dizziness or light-headedness. Otherwise, rate severity. Observation 0 not present 1 very mild 2 mild 3 moderate 4 moderately severe 5 severe 6 very severe 7 extremely severe	**ANXIETY** Ask "Do you feel nervous?" Observation 0 no anxiety, at ease 1 mildly anxious 2 3 4 moderately anxious, or guarded, so anxiety is inferred 5 6 7 equivalent to acute panic states as seen in severe delirium or acute schizophrenic reactions	**PAROXYSMAL SWEATS** Observation 0 no sweat visible 1 barely perceptible sweating, palms moist 2 3 4 beads of sweat obvious on forehead 5 6 7 drenching sweats
ORIENTATION AND CLOUDING OF SENSORIUM Ask "What day is this? Where are you? Who am I?" Observation 0 oriented and can do serial additions 1 cannot do serial additions or is uncertain about date 2 disoriented for date by no more than 2 calendar days 3 disoriented for date by more than 2 calendar days 4 disoriented for place and/or person	**VISUAL DISTURBANCES** Ask "Does the light appear to be too bright? Is its colour different? Does it hurt your eyes? Are you seeing anything that is disturbing to you? Are you seeing things you know are not there?" Observation 0 not present 1 very mild sensitivity 2 mild sensitivity 3 moderate sensitivity 4 moderately severe sensitivity 5 severe hallucinations 6 extremely severe hallucinations 7 continuous hallucinations	**AUDITORY DISTURBANCES** Ask "Are you more aware of sounds around you? Are they harsh? Do they frighten you? Are you hearing anything that is disturbing to you? Are you hearing things you know are not there?" Observation 0 not present 1 very mild harshness or ability to frighten 2 mild harshness or ability to frighten 3 moderate harshness or ability to frighten 4 moderately severe hallucinations 5 severe hallucinations 6 extremely severe hallucinations 7 continuous hallucinations

(2) SHOT scale

Sweating	0 – No visible sweating 1 – Palms moderately moist 2 – Visible beads of sweat on forehead
Hallucinations "Are you feeling, seeing, or hearing anything that is disturbing to you? Are you seeing or hearing things you know are not there?"	0 – No hallucinations 1 – Tactile hallucinations only 2 – Visual and/or auditory hallucinations
Orientation "What is the date, month, and year? Where are you? Who am I?"	0 – Oriented 1 – Disoriented to date by one month or more 2 – Disoriented to place or person
Tremor Extend arms and reach for object. Walk across hall (optional).	0 – No tremor 1 – Minimally visible tremor 2 – Mild tremor 3 – Moderate tremor 4 – Severe tremor

* False positives: Interpret SHOT with caution if patient has a febrile illness, cerebellar disease or benign essential tremor, psychosis, dementia, impaired consciousness, or delirium not related to alcohol.

Discontinuation

- Discontinue H and O if zero at baseline.
- If either H or O are greater than zero, assess and treat for delirium, encephalopathy, and/or psychosis.

History of seizures

- Diazepam 20 mg (PO/IV) or lorazepam 2–4 mg (SL/PO/IM/IV) q 1–2H x 3 doses, regardless of SHOT score.

Home management of withdrawal

Protocol

- Instruct patient to have last drink the night before
- Instruct patient to take diazepam 10 mg every 4 hours as needed for tremor (dispensed by spouse, relative, or friend)
- Prescribe no more than 60 mg diazepam
- Reassess the next day (by phone or in person)
- Clinic visit within 2–3 days

Anti-alcohol medications

Medication overview

- Anti-alcohol medications should be routinely offered to patients with AUDs. They reduce alcohol use, have a good safety profile, and help retain patients in psychosocial treatment.
- Medications:
  - Level I evidence of effectiveness: naltrexone, acamprosate
  - Level II evidence of effectiveness: topiramate, gabapentin, baclofen
- Level I medications have the strongest evidence of effectiveness; Level II medications are not officially indicated for alcohol use disorders, but have been shown to be effective in controlled trials.
- Choice of medication is based on individual considerations (such as side effects or cost).
- Titrate dose until cravings are mild and patient is abstinent, or until troublesome side effects emerge.

- If effective, prescribe for at least six months (all medications are safe for long-term use). The medication can be discontinued when patient is abstinent or has markedly reduced drinking for at least several months, has minimal cravings, has social supports and non-drug ways of coping with stress, and is confident that he or she no longer needs it to prevent relapse. The medication can be restarted again if patient does relapse.

Availability of medication

- The public formulary status of naltrexone and acamprosate varies by region:

	Naltrexone	Acamprosate
AB	Not covered	Not covered
BC	Limited coverage	Limited coverage
MB	Not covered	Not covered
NB	Special authorization	Special authorization
NL	Not covered	Special authorization
NS	Exception status	Exception status
NT	*Alcohol dependency* listed as condition with restricted benefits	
NU	*Alcohol dependency* listed as condition with restricted benefits	
ON	Exceptional status	Exceptional status
PE	Special authorization	Special authorization
QC	Covered	Exceptional medication
SK	Exception status	Exception status
YT	Covered under certain plans	Covered under certain plans
NIHB*	Covered	Limited use benefit

*The Non-Insured Health Benefits (NIHB) program covers registered First Nations persons and recognized Inuit.

- Early initiation of treatment is important because patients are at high risk for relapse and treatment drop-out in the first few weeks of abstinence; therefore, gabapentin, topiramate, or baclofen may be prescribed while waiting for approval of naltrexone or acamprosate.
- Disulfiram is only available in Canada as a compounded medication. Patients can ask their pharmacy to arrange for compounding.

Medications

1. Disulfiram (30-34)

Action

- Acetaldehyde accumulates when alcohol consumed, causing toxic reaction.
- Most effective when taken with supervision of pharmacist or family member

Side effects

- *With alcohol:* Vomiting, flushed face, and headache lasting several hours.
- *Without alcohol:* Headache, anxiety, fatigue, garlic-like taste, acne, peripheral neuropathy (with prolonged use). May cause depression.

Contraindications and precautions

- Alcohol reaction can cause severe hypotension and arrhythmias, especially in patients with heart disease or on antihypertensives.
- To avoid reaction: Wait at least 24–48 hours between last drink and first pill. Wait at least 7–10 days between last pill and first drink.
- May trigger psychosis at higher doses (500 mg). Recommended dose appears safe in schizophrenia.
- Can cause toxic hepatitis.
- Contraindicated in cirrhosis, pregnancy, and unstable cardiovascular disease.

Dose

- 125 mg PO OD usual dose.
- Increase to 250 mg if patient reports no reaction to alcohol.

2. Naltrexone (35)

Action

- Blocks opioid receptor; reduces euphoric effect of drinking.

Side effects

- Nausea, headache, dizziness, insomnia, anxiety, sedation.
- Blocks analgesic action of opioids.

Contraindications and precautions

- Pregnancy.
- Will trigger severe withdrawal in patients on opioid medications.
- Can cause reversible elevations in AST and ALT; if pre-existing liver disease, order AST and ALT at baseline and at 3-4 weeks, and discontinue naltrexone if levels rise more than 3x baseline.

Dose

- 25 mg OD x 3 days to reduce GI side effects; then 50 mg PO OD.
- Titrate to 100–150 mg per day if 50 mg has minimal effect on craving.
- Patients do not need to abstain before starting.

3. Acamprosate (36, 37)

Action

- Glutamate antagonist.
- Relieves subacute withdrawal symptoms (insomnia, dysphoria, cravings).
- Works best if abstinent several days prior to initiation.

Side effects

- Diarrhea.

Contraindications and precautions

- Renal insufficiency.
- Pregnancy.

Dose

- 666 mg tid; 333 mg tid if renal impairment or BW < 60 kg.

4. Topiramate (38-40)

Action

- Modulates GABA system.
- May improve sleep and mood disturbance in early abstinence.

Side effects

- Sedation, dose-related neurological effects (dizziness, ataxia, speech disorder, etc.) resolve over time.

Contraindications and precautions

- Can cause weight loss (risk for underweight patients).
- Lower dose needed in renal insufficiency.
- Can cause glaucoma or renal stones.

Dose

- Initial dose 50 mg OD; titrate by 50 mg to a maximum dose of 200–300 mg daily.

5. Gabapentin (41-43)

Action

- Modulates dopamine.

Side effects

- Dizziness, sedation, ataxia, nervousness.

Contraindications and precautions

- Can cause suicidal ideation (rare).

Dose

- Initial dose 300 mg bid–tid. Optimal dose is 600 mg tid.

6. Baclofen (44, 45)

Action
- GABA agonist.

Side effects
- Drowsiness, weakness, can cause or worsen depression.
- Safe in patients with liver disease.

Contraindications and precautions
- Lower dose with renal insufficiency.
- Use with caution in patients on tricyclic anti-depressants or MAO inhibitors.

Dose
- Initial dose 5 mg tid, increase to 10 mg tid. Maximum daily dose 80 mg.

Management of common outpatient alcohol-related problems

Alcohol-related mood and anxiety disorders (46)

- May be primary or alcohol-induced. Alcohol-induced disorders tend to resolve within weeks of abstinence or reduced drinking, whereas primary disorders remain the same or improve only marginally.
- Always ask patients with alcohol problems about mood, and ask patients with mood problems about alcohol.
- Treat alcohol and mood disorders concurrently.
- Consider a trial of antidepressant medication if:
  - Symptoms persist after four weeks of abstinence.
  - Unable to sustain abstinence for several weeks.
  - Possible primary mood disorder: depression precedes drinking; strong family history.
  - Severe depression (e.g., suicidal ideation).
- Long-term benzodiazepine use in heavy drinkers creates risk of accidents, overdose, and misuse.

Insomnia, non-restorative sleep

Cause	Comment	Management
Sleep apnea	May contribute to hypertension, accidents, arrhythmias.	Abstinence
Alcohol withdrawal	Can cause night-time seizures.	Abstinence Treat withdrawal
Subacute alcohol withdrawal	Common in first few weeks of abstinence.	Acamprosate, topiramate, gabapentin
Chronic night-time alcohol use	Causes rebound REM and fitful sleep.	Abstinence Trazodone, tryptophan Avoid benzodiazepines

Alcoholic liver disease

(1) Fatty liver

- First and most common phase of alcohol liver disease
- Usually asymptomatic, reversible with abstinence
- Large liver on exam and ultrasound
- Elevated GGT

(2) Alcoholic hepatitis

- Usually asymptomatic but occasionally very severe
- Diagnose elevated AST > ALT
- Advise patient that repeated and prolonged hepatitis may lead to cirrhosis

(3) Cirrhosis (47)

Risk

- Over 10–20 years, 10–20% risk of cirrhosis with 6 (men) or 3 (women) standard drinks per day

Physical signs

- Spider nevai, gynecomastia (estrogen not metabolized)
- Ascites, peripheral edema, right heart failure (low albumin, portal hypertension)
- Firm liver edge
- Splenomegaly (portal hypertension)
- Asterixis, signs of encephalopathy

Diagnostic tests

- ↑GGT (enzyme induction)
- ↑AST > ALT (alcoholic hepatitis)
- ↑INR,↑bilirubin,↓albumin (liver unable to synthesize protein)
- ↑bilirubin, low platelets (due to splenomegaly and portal hypertension)
- U/S unreliable, except if splenomegaly present (portal hypertension)
- Check for other cause of cirrhosis (e.g., hepatitis B, C)
- If concerned about encephalopathy, check serum ammonia
- Biopsy if cause uncertain

Outpatient management

(a) Prevent progression

- Abstinence
  - 5-year survival in cirrhosis with complications: abstainers 60%, non-abstainers 34%.
  - Risk of variceal bleed 10 times greater with recent heavy drinking than with abstinence
  - Abstinence crucial if hepatitis C positive
- Avoid NSAIDs and limit acetaminophen to 2–3 g daily (only as necessary; patient must be abstinent).

(b) Liver transplant

- Most effective treatment for cirrhosis
- To get on transplant list, patients require 6 months to 2 years of abstinence as well as a treatment program

(c) Encephalopathy

- Avoid benzodiazepines; use caution with other sedating drugs
- Lactulose (30–45 mL orally 3 times a day) if at high risk or early signs: poor concentration, day-night reversal, inattention, slow responses.
- Urgent intervention for triggers: electrolyte imbalance, blood loss, high protein meal, benzodiazepines, infection

(d) Ascites

- Low salt diet
- Moderate fluid intake
- Judicious use of diuretics (e.g., spironolactone)

(e) Portal hypertension

- Regular endoscopic measurement of portal pressures
- Nadolol if portal hypertension

Hypertension

- Consumption of 3+ standard drinks/day can cause or exacerbate hypertension.
- Patients with alcohol-induced hypertension tend to be refractory to antihypertensive medication.
- Hypertension resolves within weeks of abstinence or reduced drinking.

Neurological conditions

- Alcohol-induced dementia, cerebellar ataxia, peripheral neuropathy, parkinsonism
- Conditions often improve with abstinence over weeks/months

Dilated cardiomyopathy

- Presents with heart failure and arrhythmias
- Excellent prognosis; sometimes completely resolves within months of abstinence

GI bleed

- Gastritis, esophagitis: abstinence, PPI
- Esophageal varices: abstinence, treatment of portal hypertension, treatment of cirrhosis

Prescribing benzodiazepines and opioids (48)

- Risk of overdose and accidents greatly increased when combining benzodiazepines or opioids with alcohol.
- Both medications should be routinely tapered to the lowest effective dose in the elderly.

Reporting to the Ministry of Transportation

Suggested criteria for reporting

- Patient admits to drinking and driving.
- Family member informs you that patient is drinking and driving.
- Patient drinks steadily throughout the day and regularly drives.
- Patient drove to your clinic while intoxicated.
- Patient regularly drives and has recently experienced severe withdrawal or complication of withdrawal (e.g., seizure).
- Patient has blackouts caused by alcohol consumption.
- Patient has other alcohol-related complications that impair driving ability (e.g., cerebellar ataxia, recurrent trauma, sleep apnea, on high doses of opioids or benzodiazepines, hepatic encephalopathy).

Management of patients with suspended licenses

- Explain to the patient that you have a legal obligation to report.
- Patients may ask you to give them a chance to abstain and attend treatment before deciding to report them.
- However, trusting the patient to comply with your instructions is not considered an adequate reason for failing to report. Therefore, take the following precautions when delaying reporting:
  - Inform the patient that you will report if patient misses follow-up appointments or if monitoring or history suggests ongoing drinking.
  - Order GGT and MCV regularly.
  - Consider urine ethyl glucuronide every 1–2 weeks; EG detects alcohol consumption for several days after last drink.
  - Check urine creatinine to detect tampering.
- To lift the suspension, the patient must have attended treatment and maintained abstinence or low-risk drinking for a specified number of months (usually one year).
- Monthly appointments are recommended. At each appointment:
  - Ask about alcohol consumption and attendance at AA and treatment programs.
  - Order GGT and MCV.
  - With the patient's permission, ask the spouse/partner or close family member to corroborate the patient's reported alcohol consumption.
- Write follow-up letter to Ministry if patient is abstinent at 6 months and at one year.

Part III: Opioids

Introduction

Opioids have long been an important tool in the treatment of acute and chronic pain. Since the 1990s, Canadian physicians have dramatically increased their opioid prescribing. This has benefited many patients with chronic non-cancer pain (CNCP), but it has also been associated with substantial increases in opioid overdose deaths and opioid use disorders (49, 50). Evidence suggests that physicians' prescribing practices, which were influenced by aggressive marketing of opioids by pharmaceutical companies during the 1990s (51, 52), are a major contributor to these harms (53-57). The medical profession has responded to this public health crisis by developing a set of evidence-based guidelines and best practices on opioid prescribing for chronic pain, originally published in 2010 (58) and revised in 2017 (59). However, many family physicians continue to experience discomfort or a lack of confidence about how to prescribe opioids safely, and most do not know how to manage harms related to both licit and illicit opioid use. As well, it is only since 2012 that the *Controlled Drugs and Substances Act* has enabled Canadian nurse practitioners to prescribe opioid medications. This section outlines the role of opioids in acute pain and CNCP management, provides a clear protocol for initiating and monitoring long-term opioid therapy, and advises on how to reduce, mitigate, or prevent the harms associated with chronic opioid use.

We have made every effort to take into account current developments in the opioid field, particularly the 2017 opioid guidelines. We have attempted to interpret the guidelines' broad recommendations to reflect individual patients' clinical

circumstances. These interpretations are highlighted where they occur; practitioners are encouraged to consider the individual needs of patients when making clinical decisions.

Opioids for acute pain (60)

Indications for opioid treatment

- Moderate to severe acute pain that has not responded a trial, of adequate dose and duration, of all evidence-based non-opioid treatments (e.g., acetaminophen, SNRIs, NSAIDs, physiotherapy)

Contraindications to opioid treatment

- Mild acute pain (e.g., low back pain, dental pain, muscle strains)
- Active substance use disorder

Protocol for opioid prescribing

- Use **lowest effective dose** of **immediate-release** formulation, preferably combined with a non-opioid medication (e.g., codeine + acetaminophen).
- Prescribe only enough to last for expected duration of severe pain (usually 3–7 days).

Initiating opioid therapy for CNCP

Indications for opioid trial

- Patient has a well-defined pain condition (nociceptive or neuropathic) that (a) has been shown to respond to opioids, and (b) causes both **pain and disability**.

- Diagnosis is confirmed on physical examination, diagnostic imagining, and/or consultation.
- Non-opioid treatments are contraindicated, have intolerable side effects, or are found to be ineffective after an **adequate trial** (e.g., one month for SNRIs).
- Opioids are usually not effective in conditions where central sensitization has occurred (e.g., fibromyalgia, tension headaches, IBS).
- Systematic review (61) found that opioids provide minimal analgesic benefit for low back pain overall, and this benefit is outweighed by opioid side effects.

Precautions and contraindications to opioid trial

- Use caution when prescribing opioids to patients with a current, active psychiatric disorder (i.e., anxiety disorder, mood disorder, post-traumatic stress disorder).[1]
- Avoid long-term opioid therapy in patients with current, recent, or severe past history of problematic use of alcohol, opioids, cannabis, or other substances.[2]

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[1] The 2017 opioid guidelines recommend that active psychiatric disorders be stabilized before an opioid trial is considered. However, we suggest that patients with an active psychiatric disorder be considered for a carefully monitored trial of opioid therapy, if they have a severe nociceptive or neuropathic pain condition that impairs daily functioning and has not responded to an adequate trial of all standard non-opioid treatments. The patient should also receive concurrent treatment for their psychiatric disorder. If you decide to initiate a trial of opioids, monitor the patient closely to assess benefits, adverse effects, and signs of misuse.

[2] The 2017 opioid guidelines recommend that opioids not be prescribed to patients with any history of problematic substance use. However, an opioid trial may be indicated for severe pain that has not responded to other treatment modalities if the history of problematic substance use is remote and not severe.

Prior to prescribing opioids

- Ask about current and past use of alcohol and drugs.
- Ask about mood. Depressed patients tend to have a heightened perception of pain and are less responsive to opioid therapy.
- Check renal and respiratory status, especially risk of sleep apnea.
- In elderly patients, assess risk of falls.
- Consider tapering benzodiazepines (see page 102).
- Ask about the impact of pain on activities of daily living, e.g., walking, cooking, visits to family and friends.
- Have the patient rate the severity of their pain on a 0–10 scale, at rest and with activity.
- Reassess their response to non-opioid treatments:
  - Nociceptive pain: acetaminophen, NSAIDs, SNRIs
  - Neuropathic pain: anticonvulsants, SNRIs, TCAs
  - All pain: Mindfulness programs, graded exercise
- Inform patients that opioid therapy will be a **trial**, to be discontinued if side effects outweigh benefits.
- Advise patients not to drink alcohol during titration.
- Warn patients to avoid driving for at least two hours after a dose in the first 1–2 weeks of treatment initiation and the first week of dose increase.
- Warn patients to keep their opioids safely stored, and not to give any opioid medications to relatives or friends.

Office visits

- See the patient frequently during initiation and titration.
- At each office visit, ask about changes in:
  - Work, school, social activities, daily activities
  - Pain ratings on a 0–10 scale, at rest and with activity
  - Mood
- Ask about side effects:
  - Sedation, dizziness, and other CNS effects
  - Constipation, nausea

Opioid prescribing protocol

Immediate release (IR) vs. controlled release (CR)

- Initiate opioid trial with IR preparations.[3]
- Maintain on IR for brief pain (less than 4 hours) or incident pain (triggered by activity).
- For constant pain throughout the day, switch to CR.
- In long-term therapy for constant pain throughout the day, IR preparations should not exceed 10–30% of total daily opioid dose.

Opioid selection

- Always initiate opioid treatment with weak opioids, i.e., oral codeine, tramadol, or buprenorphine patch. These medications are effective and have much lower risk of overdose, addiction, sedation, and falls than potent opioids.

[3] We concur with the 2017 opioid guidelines regarding the use of CR opioids for constant pain throughout the day; however, as CR formulations are generally very potent, we recommend using IR preparations during initiation and titration in order to minimize the risk of acute toxicity.

- If insufficient analgesia with first-line opioids, prescribe morphine, oxycodone, or hydromorphone.
- Morphine is contraindicated in patients with renal insufficiency.
- Evidence suggests that hydromorphone and oxycodone have fewer cognitive effects than morphine in the elderly.
- Transdermal fentanyl should be avoided if possible in the elderly and in patients with less severe pain. It is very easy to overdose on the patch. Use only if the patient has taken at least 60–100 mg morphine equivalent (MEQ) daily for at least 2 weeks.

Opioid initiation and dose titration

Opioid*	**Max initial dose****	**Max dose increase**	**Min days between increases**	**Min IR dose before CR**
Codeine	200 mg/d	50 mg/d	7 days IR 14 days CR	150 mg
Transdermal buprenorphine	5 µg/7d	5 µg/7d	7 days	-------
Morphine	40 mg/d	10 mg/d	7 days IR 14 days CR	30 mg
Oxycodone	30 mg/d	5 mg/d IR 10 mg/d CR	7 days IR 14 days CR	20 mg
Hydromorphone	8 mg/d	1–2 mg/d IR 2–4 mg/d CR	7 days IR 14 days CR	6 mg
Tapentadol***	150 mg/d	50 mg/d IR 50 mg/d CR	7 days IR 14 days CR	100 mg

* Potent opioids should only be dispensed to patients currently taking weak opioids daily. All dose increases should be based on an individual assessment.
** Starting dose is 40 mg MEQ (less for seniors).
*** Maximum CR dose 250 mg bid. Exert caution when switching from pure mu-opioids.

Morphine equivalency

Opioid	Approximate equivalence value
Morphine (reference)	30 mg
Codeine	200 mg
Oxycodone	20 mg
Hydromorphone	6 mg
Tapentadol	100 mg
Transdermal buprenorphine	No equivalence to morphine established
Transdermal fentanyl	25 μg/hr = 60–134 mg oral morphine/day

Optimal dose

- Effective opioid therapy causes gradual improvement in pain and function as dose increases.
- Optimal dose reached if:
  - Pain relief at least 2 points on 10-point scale, with no benefit from 1–2 additional increases.
  - Improved functioning at work, school, and with family; increased physical activities.
  - No major side effects.
- Most patients respond to a dose of **50 mg MEQ or less**; doses above 90 mg MEQ are rarely needed.
- In some cases, referral for a second opinion regarding the possibility of increasing the dose to more than 90 mg MEQ may be necessary.

Ongoing vigilance

- Opioids have dose-related complications, including overdose, sleep apnea, and falls and fractures.
- Any patient with an ongoing opioid prescription of 40 mg MEQ or more should have **monthly visits** to assess:
  - Pain levels, at rest and with activity
  - Function (mood, activities of daily living)
  - Adverse effects
- At doses of 90+ mg MEQ, the prescriber should reassess the opioid's analgesic effectiveness and side effects, and decide whether to maintain the dose or taper.[4]

Minimizing adverse effects

(a) Falls in the elderly

- Do not prescribe opioids to cognitively impaired patients unless dispensed and overseen by a caregiver.
- Taper benzodiazepines (see page 103).
- Benzodiazepines increase risk and severity of opioid-induced fatigue, sedation, inattention and overdose.
- Avoid use of opioids at night if possible.
- If pain wakes the patient up, prescribe the smallest IR opioid dose and warn patients to take extra precautions when getting out of bed.

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[4] The 2017 opioid guidelines recommend that all patients on doses of 90 mg MEQ or higher be tapered. While it is true that the dangers associated with opioid therapy are dose-related, we believe that the decision to taper should be based on the patient's pain, functioning, and adverse effects in addition to the dose. All patients on long-term opioid therapy should be monitored for their response to the treatment, and tapering should be considered for any patient showing adverse effects or insufficient benefit, regardless of the dose. Tapering should be prioritized in patients who have received insufficient analgesia from opioids, who are suffering from opioid-related complications, or patients with an opioid use disorder for whom opioid substitution therapy is contraindicated.

(b) Sedation during initiation or dose increase

- Sedation, slowed speech, or "nodding off" are all early signs of an impending overdose.
- The patient may appear relatively alert in conversation, yet have respiratory arrest at night while asleep.
- Family members should contact the care provider or call emergency services at the first sign of an overdose.

(c) Fatigue

- Opioids can cause fatigue either through a direct sedating effect or by contributing to sleep apnea.
- Patients who report daytime fatigue and/or reduced function should be assessed for sleep apnea. Their opioid dose should be reduced or discontinued, or the opioid should be switched.

(d) Constipation

- Use a stepped approach:
  - Start with dietary fibre, adequate fluid, and activity.
  - Progress to osmotic laxatives (polyethylene glycol, sodium picosulphate, or lactulose).
  - Progress to stimulant laxatives (bisacodyl, senna).
  - Progress to peripheral opioid receptor antagonists (combination oxycodone-naloxone, a-methyl naltrexone, naloxegol).

Opioid switching

Indications for opioid switching

- Inadequate analgesic response to the current opioid (pain relief < 2/10, no improvement in function) despite a reasonable dose (e.g., 60 mg MEQ). Patients who have had minimal analgesic response to a moderate dose are unlikely to benefit from further dose increases.
- Adverse effects with the current opioid, e.g., constipation, sedation, falls.
- Potential tapering strategy.

Opioid switching protocol

- Because the patient will not be fully tolerant to the new opioid, the MEQ should be 50% of the MEQ of original.
- *Example:* When switching a patient from 40 mg/d of oxycodone to hydromorphone:
  - 40 mg/d oxycodone = 60 mg MEQ
  - 60 mg MEQ = 12 mg/d hydromorphone
  - 50% of hydromorphone 12 mg = 6 mg
  - Therefore, start patient on 6 mg/d in divided doses.
- Emphasize that taking extra doses is dangerous.
- Titrate dose as described on page 48.

Opioid tapering

Rationale for opioid tapering

- Tapering is an **active therapeutic decision** made for the patient's benefit when they have failed at opioid therapy.
- Evidence suggests that tapering after a failed opioid trial improves pain, mood, and functioning.
- Tapering is **far safer** than abrupt cessation:[5]
  - Abrupt cessation will trigger severe withdrawal, and patients will lose their opioid tolerance within days, creating a heightened risk of overdose.
  - Abrupt cessation can also lead patients seek illicit sources of opioids, which can result in accidental exposure to fentanyl.

Indications for opioid tapering

- Patient has persistent severe pain and pain-related disability despite an adequate opioid dose (e.g., 60 mg/d MEQ), and the patient has already failed on a trial of at least one opioid previously.
- Patient is on an unusually high dose for pain condition (well above 90 mg MEQ for mechanical low back pain).
- Patient has a complication from opioid therapy, such as sleep apnea, sedation, or dysphoria.
- Patient has suspected opioid use disorder and opioid maintenance therapy is not an option.

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[5] The 2017 opioid guidelines present very rapid or immediate cessation of opioid therapy as an alternative method of tapering; however, we strongly recommend against this practice. The guidelines advise that this be done in a medically supervised withdrawal centre, but this does not mitigate the risk of subsequent relapse and overdose due to loss of tolerance. If a patient needs to discontinue their opioids more rapidly than a standard taper allows, they should be switched to opioid maintenance therapy.

Reluctance to taper

If patient expresses reluctance to taper their opioid dose:

- Explain **why** you are tapering the opioid dose: to prevent future harms (e.g., falls) and to improve the patient's mood and well-being (e.g., energy and sleep).
- Explain that tapering does not usually increase pain, and may actually improve it:
  - Opioids often stop working after many months or years.
  - Opioids can even make pain worse by lowering the pain threshold.
- Explain that you are not necessarily going to stop the opioids altogether, but lower it to a safer dose that improves mood and function while still keeping the pain manageable.
- Explain that you will be lowering the dose **gradually**, and that you will adjust the rate of the taper according to how the patient is doing.

Failed taper

A *failed taper* occurs when the patient persistently refuses to taper the dose further due to severe pain. A failed taper may occur for several reasons:

- Patient has an underlying opioid use disorder and cannot tolerate even small reductions in the opioid dose.
- The taper was done too quickly and/or the patient is suffering from end-dose withdrawal symptoms.
- The patient's pain condition responds to a higher dose.

In response to a failed taper, the prescriber has the following options:

- Switch to buprenorphine/naloxone. While this is particularly important for patients with an underlying opioid use disorder, it can also be helpful in other patients, as the long duration of action of buprenorphine often makes the taper more tolerable.
- Hold the taper and refer patient to a multidisciplinary pain program (if available).

Tapering protocol

Formulation	CR preferred (until low dose reached).
Dosing interval	Scheduled doses rather than PRN Keep dosing interval the same for as long as possible (bid or tid). Advise patients not to skip doses.
Rate of taper	Taper slowly, typically 10% of the total daily dose at each office visit, no more than 10% of total daily dose **every 1–2 weeks**. Adjust rate of taper according to patient's pain and withdrawal symptoms. If patient experiences mild withdrawal symptoms, reassure them they will resolve after 1–2 weeks. Let patient choose which dose is decreased (AM, PM, or HS). Taper even more slowly when 1/3 of total dose is reached.
Dispensing interval	If patient runs out early, increase frequency to weekly, alternate day, or daily.
Endpoint of taper	Dose well below 90 mg MEQ. Controls pain with minimal side effects. Similar or improved mood and function.
Frequency of visits	If possible, see patient prior to each dose decrease.
Approach at each visit	Ask not just about withdrawal symptoms but benefits of tapering: more alert, less fatigued, improved mood, improved pain, etc. If pain persists, consider referral to a multidisciplinary program (if available) if the patient does not show signs of opioid misuse or use disorder.[6]

[6] The 2017 opioid guidelines recommend that patients showing behaviours indicating opioid misuse or use disorder be referred to a multidisciplinary program. However, patients displaying these behaviours should first be assessed for an opioid use disorder; in these patients, opioid maintenance therapy with methadone or buprenorphine/naloxone is likely to improve pain and functioning.

Opioid misuse

Limiting diversion

- Warn patients to store their medication in a locked box or other secure location, not to show them to younger relatives, and not to share them with anyone.
- Avoid using fentanyl patches in elderly patients with younger adults at home (patches can be easily lifted off the skin of a sleeping patient).
- Consider a fentanyl patch exchange program (http://www.patch4patch.ca).
- Without anyone else in the office, ask parents and grandparents on opioids if younger relatives could be using their medication, especially if the patient requires high doses, runs out early, or is accompanied by a younger adult to the office visits.
- Use part fill prescriptions. The 2017 opioid guidelines suggest a maximum of 28 days, but in patients with personal or environmental risk factors, weekly or two-week prescriptions may be appropriate.

Monitoring for misuse

- Any patient with an ongoing opioid prescription of 40 mg MEQ or more should be monitored for signs of misuse.
- At each visit, the clinician should assess the patient for:
  - Changes in their mood, relationships, or functioning
  - Concerns expressed by family or close friends
  - Unauthorized changes to dose, schedule (i.e., binge use), or route of delivery (e.g., biting oral tablets)
  - Euphoric effects (e.g., relaxation, confidence, energy) immediately after taking a dose
  - Withdrawal symptoms

    - Drug-seeking behaviours: running out of medication early, frequent requests for dose increases, etc.
- These features may indicate that the patient is at risk for an **opioid use disorder** (see below).

Opioid use disorder (OUD)

The DSM-V gives the following criteria for an OUD (17):

(a) Opioids taken in larger amounts or over a longer period of time than intended.
(b) Repeated unsuccessful efforts to reduce use.
(c) Great deal of time spent obtaining or using opioids, or recovering from their effects.
(d) Strong cravings or urges to use opioids.
(e) Recurrent opioid use resulting in a failure to fulfill major responsibilities.
(f) Continued use despite opioid-related social or interpersonal problems.
(g) Reduction of major activities because of opioids (e.g., missing work, spending less time with children or spouse).
(h) Repeatedly using opioids in situations or activities where intoxication is dangerous.
(i) Continued use despite knowledge of opioid-related physical or psychological problems.
(j) Tolerance (need to use more to achieve the same effect, or diminished effects with continued use of the same amount).
(k) Withdrawal (e.g., myalgias, chills, sweating, nausea/vomiting, cramps, diarrhea, insomnia, anxiety, dysphoria).

Patients who meet two or three of these criteria have a **mild** OUD, four to five criteria indicate a **moderate** OUD, and six or more indicate a **severe** OUD.

Symptoms, signs, and behaviours

OUDs are difficult to diagnose; patients are often reluctant to disclose key symptoms and behaviours for fear that the practitioner will discontinue the opioid. A diagnosis often requires collateral information from family members and observation of a pattern of behaviour over time. The following patterns tend to emerge in patients with an OUD:

- Patient's opioid dose high for underlying pain condition
- Aberrant behaviours: Running out early, crushing or biting oral tabs, or accessing opioids from other sources
- Strong resistance to tapering or switching current opioid
- Importance patient attaches to the drug far outweighs its analgesic benefit (e.g., "pain is 10/10, hydromorphone only takes edge off, but I would die if you stopped it")
- Binge rather than scheduled opioid use
- May be currently addicted to other drugs, e.g., alcohol
- Depressed and anxious
- Deteriorating mood and functioning
- Concerns expressed by family members
- Reports recurrent, frightening withdrawal symptoms
- May acknowledge that they experience immediate improvement in mood after taking the opioid

Harm reduction advice

All patients with a suspected OUD should be given advice on harm reduction and reducing the chance of a fatal overdose:

- Never use opioids alone; always use with a friend and make sure you are both aware of the signs of overdose (pinpoint pupils, falling asleep, slowed or stopped breathing, bluish skin around lips or under nails).
- If a friend has overdosed:
  - Shake them and call their name.
  - Call 911.
  - Administer naloxone and start chest compressions.
  - If they are drowsy and nodding off but not unconscious, do not let them fall asleep; keep talking to them until they are awake and alert for at least an hour without slurred speech/nodding off. If they cannot remain alert, take them to the ED.
- If you are taking opioids after a period of abstinence of any length, take a much smaller dose than you used to.
- Be aware that drug dealers often add fentanyl to their product without informing their customers. Only medications obtained from a prescription and purchased at a pharmacy are guaranteed to be free of fentanyl.
  - Fentanyl is many times more potent than heroin.
  - Even a tiny amount and kill a heavy and experienced opioid user.
- Do not inject opioids.
- Do not mix opioids with other substances, especially alcohol or benzodiazepines.
- Always carry naloxone (see page 61).
- The only sure way to prevent overdose is to stop using. The most effective way to do this is through opioid maintenance therapy (see page 65).

Take-home naloxone

Naloxone is a competitive opioid antagonist with a duration of action of 15–30 minutes. Take-home naloxone is available in two bioequivalent formulations: parenteral naloxone 0.4 mg and intranasal naloxone 4 mg. The latter is much more expensive but is more acceptable to oral opioid users. In most provinces, public health departments offer naloxone kits and training through their needle exchange programs, and some provinces have made parenteral and/or intranasal naloxone available at community pharmacies at no charge and without a prescription.

Indications for naloxone

- On a high dose of prescription opioids (200+ mg MED)
- On prescription opioids and also taking benzodiazepines or drinking heavily.
- Previous overdose
- Suspected OUD
- Intermittent recreational use or illicit opioids
- Has regular contact with friends or relatives who have OUD
- Heavy users of cocaine or other non-opioid drugs (drug dealers sometimes add fentanyl to non-opioid drugs)

When giving or recommending naloxone, the clinician should spend a few minutes advising the patient on overdose prevention (see page 60). This advice will reinforce the education they will receive from the public department or pharmacy.

Options for management of OUDs

(a) Abstinence-based psychosocial treatment

Abstinence-based treatment is the cessation of all alcohol and drugs, including methadone and buprenorphine/naloxone; it is usually accompanied by psychosocial interventions, such as counselling or self-help groups (e.g., Narcotics Anonymous). This form of treatment is **less effective than opioid maintenance therapy** but often preferred by patients. Patients are at increased risk for opioid overdose after leaving abstinence-based programs, so it is crucial that they are given harm reduction advice and overdose prevention strategies (see pages 60–61).

(b) Structured opioid therapy

Structured opioid therapy is continued opioid prescribing under conditions that limit misuse. Preliminary evidence suggests it is effective, convenient for patients, and easier to organize than opioid substitution therapy. Refer patients for opioid substitution therapy if structured therapy fails.

Indications

- Has or is at high risk for opioid use disorder (younger, personal or strong family history of addiction, anxiety or mood disorder).
- Has pain condition requiring opioid therapy.
- Only uses opioids supplied by one prescriber.
- Does not alter route of delivery (inject or crush oral tabs).
- Is not currently addicted to alcohol or other drugs.

Protocol

- Perform taper (see page 53).
- Dispense small amounts frequently (e.g., 1–2 times per week).

- Do not refill if patient runs out early.
- Monitor closely with urine drug screens, pill counts, office visits.
- Switch to buprenorphine/naloxone or methadone treatment if structured opioid therapy fails (e.g., patient continues to access opioids from other sources).

(c) Involuntary taper

Opioid tapering is often difficult for people with moderate to severe OUDs; they usually experience intense and frightening withdrawal symptoms along with powerful cravings, leading them to access illicit opioids. Although opioid maintenance therapy with methadone or buprenorphine/naloxone (see page 65) is indicated in these cases, patients may be resistant to this treatment. In this situation, the patient should be slowly tapered off their opioid.

Tapering gives the patient several weeks or months to consider and make an informed decision about the need for opioid substitution treatment. As well, tapering is safer to the patient and the public than ongoing prescribing of high doses or abrupt cessation. The former allows the patient to put off treatment indefinitely, maintaining the risk of diversion and overdose; the latter will cause the patient to lose tolerance, increasing their risk of overdose.

Note that you should not discharge patients with OUDs from your practice unless they have been abusive towards you, your staff, or other patients, or if you have concrete evidence that they have been selling your medications.

Indications

- Has an opioid use disorder (if you are unsure about the diagnosis, consult with an addiction physician or pain physician who is knowledgeable about OUDs).
- Does not have a pain condition requiring long-term opioid therapy.
- Suspected of injecting, crushing, or snorting oral tabs.
- Suspected of accessing opioids from more than one source (either double-doctoring or purchasing from the street) or of selling their medication.

Patient reluctance

If the patient expresses resistance to an involuntary taper, deliver the following message:

> You have an opioid use disorder. The opioid I am prescribing may be making it harder for you to function and may be worsening your mood. It is also putting you at risk of serious harm, including death from overdose.
>
> The most effective treatment for opioid use disorder is opioid maintenance treatment. This treatment will result in improved mood, function, and pain. It will eliminate your cravings and withdrawal symptoms. However, since this is not an option at this time, your opioid dose needs to be lowered for safety reasons. As you will lose tolerance as the dose is lowered, it is important that you take steps to prevent opioid overdose (see pages 60–61).
>
> If you change your mind about opioid maintenance therapy at any point, I will arrange treatment for you, either with me or at an addiction clinic. If you disagree with this decision, please feel free to find another care provider. Until then, we will proceed with the taper.

Protocol

- Provide patient with naloxone and advice on harm reduction.
- Dispense frequently (as often as daily).
- Taper by 10% of total baseline dose per week (e.g., if patient is on 600 mg MED, taper by 60 mg per week).
- Slow taper to 10% every 2 weeks once dose of 200 mg MEQ is reached.
- See the patient frequently, every 1–2 weeks.
    - During each visit, emphasize that opioid maintenance therapy with methadone or buprenorphine/naloxone will relieve their withdrawal symptoms while improving their mood and function.
    - If patient agrees to opioid maintenance therapy, refer to addiction physician or initiate buprenorphine/naloxone treatment (see below).
- Taper completely off opioid.
    - If patient has a severe biomedical pain condition that warrants opioid therapy, prescribe once-daily long-acting morphine, daily dispensed, at a maximum dose of 50 mg.

(d) Opioid maintenance therapy

Opioid maintenance therapy is substituting an illegal and/or euphoria-inducing opioid with a longer-acting, less euphoric opioid (i.e., methadone or buprenorphine/naloxone). While all methadone prescribers in Canada are required to have an exemption under section 56 of the *Controlled Drugs and Substances Act*, each province and territory has its own requirements about prescribing buprenorphine/naloxone:

AB	Approved training course required
BC	Indivior[7] training course recommended
MB	Methadone exemption required Indivior training course required
NB	Formal approval not required Evidence of training may be requested
NL	Training course strongly recommended
NS	Centre for Addiction and Mental Health training course required
NT	No known requirements
NU	Prescribers must provide proof of competence
ON	Training course recommended One-day clinical observership recommended Ongoing continuing medical education recommended
PE	Indivior training course required Course on fundamentals of addiction medicine required within first two years Minimum of 20 hours of formal continuing medical education in addiction medicine required every five years
QC	Indivior training course required Additional day-long training course required
SK	Methadone exemption required Approved training course required Six hours of formal continuing medical education in addiction medicine required every two years
YT	No requirements

Indications

- Has an OUD.
- Failed at opioid tapering.
- Currently misusing alcohol or other drugs.

[7] Indivior is the manufacturer of brand-name buprenorphine/naloxone.

Prescribing buprenorphine/naloxone

Buprenorphine

- Partial opioid agonist with a ceiling effect.
  - Unlike full agonists such as morphine, even very high doses rarely cause respiratory depression unless combined with alcohol or sedating drugs.
- When taken in the appropriate dose, relieves withdrawal symptoms and cravings for 24 hours without causing euphoria.
- Binds very tightly to the opioid receptors, displacing other opioids that occupy the receptor site; this minimizes the psychoactive effect of other opioids taken concurrently.
- Has a slow onset and long duration of action because it dissociates very slowly from the receptors.
- Side effects similar to those of other opioids: nausea, constipation, and sedation.
- Buprenorphine is often combined 4:1 with naloxone, an opioid antagonist, in order to prevent misuse: the naloxone in the preparation has no effect when taken sublingually, but will trigger severe withdrawal if injected.

Initiation protocol

- Ensure that patient has no opioid in their serum before taking the first dose.
  - Buprenorphine/naloxone is very safe, even in patients who have never taken it before, but it does displace opioids currently attached to the receptor.
  - This precipitates opioid withdrawal in patients who are physically dependent on those opioids.
  - Precipitated withdrawal is rarely severe or dangerous, but patients who experience it are reluctant to try buprenorphine/naloxone again.
  - Use the Clinical Opioid Withdrawal Scale (COWS) to gauge the patient's withdrawal:

Clinical Opioid Withdrawal Scale (COWS) (62)

Interval	0	30m	2h	4h
Date **Time**				
	Score	**Score**	**Score**	**Score**
Resting heart rate (measure after lying or sitting for one minute): **0** HR ≤ 80 **2** HR 101–120 **1** HR 81–100 **4** HR > 120				
Sweating (preceding 30m and not related to room temp/activity): **0** no report of chills or flushing **1** subjective report of chills or flushing **2** flushed or observable moistness on face **3** beads of sweat on brow or face **4** sweat streaming off face				
Restlessness (observe during assessment): **0** able to sit still **1** reports difficulty sitting still, but is able to do so **3** frequent shifting or extraneous movements of legs/arms **5** unable to sit still for more than a few seconds				
Pupil size: **0** pupils pinned or normal size for room light **1** pupils larger than normal for room light **2** pupils moderately dilated **5** pupils so dilated that only the rim of the iris is visible				

Interval	0	30m	2h	4h
Date **Time**				
	Score	**Score**	**Score**	**Score**
Bone or joint pain (not including existing joint pains): **0** not present **1** mild diffuse discomfort **2** patient reports severe diffuse aching of joints/ muscles **4** patient is rubbing joints / muscles plus unable to sit still due to discomfort				
Runny nose or tearing (not related to URTI or allergies): **0** not present **1** nasal stuffiness or unusually moist eyes **2** nose running or tearing **4** nose constantly running or tears streaming down cheeks				
GI upset (over last 30 minutes): **0** no GI symptoms **1** stomach cramps **2** nausea or loose stool **3** vomiting or diarrhoea **5** multiple episodes of vomiting or diarrhoea				
Tremor (observe outstretched hands): **0** no tremor **1** tremor can be felt, but not observed **2** slight tremor observable **4** gross tremor or muscle twitching				
Yawning (observe during assessment): **0** no yawning **1** yawning once or twice during assessment **2** yawning 3+ times during assessment **4** yawning several times/minute				
Anxiety or irritability **0** none **1** patient reports increasing irritability or anxiousness **2** patient obviously irritable or anxious **4** patient so irritable or anxious that participation in the assessment is difficult				
Gooseflesh skin **0** skin is smooth **3** piloerection (goosebumps) of skin can be felt or hairs standing up on arms **5** prominent piloerection				
SCORE INTERPRETATION	Total	Total	Total	Total
5–12 MILD 13–24 MODERATE 25–36 MODERATELY SEVERE > 36 SEVERE	Initials	Initials	Initials	Initials

- Office induction is preferred, as it will ensure patient does not go into precipitated withdrawal.
- Home induction may be necessary in certain situations:
  - Patient is unable to abstain from opioids long enough to attend the office in withdrawal.
  - Patient is at high risk for treatment drop-out (e.g., younger, injection opioid user, unstable housing).
  - Patient is in an acute care setting (e.g., ED, withdrawal management), is not yet in withdrawal, and is unlikely to keep a clinic appointment.
- **Office induction protocol:**
  - At least 12 hours since last oral IR dose, 24 hours since last oral CR dose.
  - Patient reports typical withdrawal symptoms.
  - COWS score of 12+
  - First dose: 4 mg SL. Dose may take several minutes to dissolve.
  - Reassess in 2 hours. If patient improved but still in withdrawal, give another 4 mg to take in office or at home. **Maximum dose first day** is **12 mg**.
- **Home induction protocol:**
  - Prescribe 2 mg SL q4H PRN, up to 6 tabs over 24 hours, x 1–3 days (e.g., 18 tabs all as take-home or 6 tabs daily dispensed for 3 days).
  - Warn patient to wait at least 12 hours after last opioid use and be in at least moderate withdrawal before taking first dose.
  - Take 2 mg x 2 tabs SL.
  - If still in withdrawal after 2 hours, take another 2 mg x 2 tabs SL. **Maximum dose** is **12 mg** in 24 hours.

Titration

- Reassess in 1–3 days. Increase dose by 2–4 mg at each visit if patient reports withdrawal symptoms or cravings towards the end of a dosing interval. Each dose increase should increase duration of relief from withdrawal and cravings.
- **Optimal maintenance dose** is usually **8–16 mg SL OD**; **maximum dose** is **24 mg SL OD**. The optimal dose should relieve withdrawal symptoms and cravings for 24 hours without causing significant sedation or other side effects.
- If feasible, at the beginning of therapy, buprenorphine/naloxone should be dispensed daily under observation by the pharmacist.
    - This is particularly important if the patient has been accessing opioids from other sources.
    - If the patient is unable to attend daily because of limited mobility, lack of transportation, or work or family commitments, arrange supervised dispensing at home by a nurse or reliable relative.
    - Take-home doses may be prescribed once patient is at optimal dose and has stopped unauthorized use.
- Arrange frequent office visits for counseling and urine drug screen monitoring.

Buprenorphine/naloxone prescriptions

Prescription should include:

- Patient's name, date of birth, and health card number
- The pharmacy address and fax number
- The dose
- Start and end dates
- Day(s) of the week the patient takes a dose at the pharmacy under the observation of the pharmacist, and days of the week the patient takes the dose at home. Stable patients usually attend the pharmacy once a week to take a single dose under the observation of a pharmacist and receive 6 tablets to take home.

The cost of generic buprenorphine/naloxone is covered on the provincial formularies of Alberta, British Columbia, Manitoba, Newfoundland and Labrador, Ontario, and Québec. In the other provinces and territories, as well as on the Non-Insured Health Benefit (NIHB) plan, special authorization is required for coverage.

Follow-up visits for stable patients on buprenorphine/naloxone

- Ask about withdrawal symptoms or cravings; sometimes patients require minor dose adjustments of 2–4 mg/day.
- Ask about alcohol and cannabis use.
- Ask about overall mood and functioning.
- Manage chronic medical conditions (e.g., hepatitis C) or psychiatric conditions (e.g., anxiety, depression).
- Perform regular screening and health maintenance (e.g., pap tests, mammograms, immunizations, etc.).
- Identify any new medical or psychiatric conditions.

- Review urine drug screen results.
  - Stable patients should leave at least one urine sample per month.
  - Review unexpected results with patient and, if necessary, with addiction physician.

Interpretation of unexpected urine drug screen results

Result	Interpretation	Action
Absence of norbuprenorphine	Noncompliance or diversion	If diversion suspected, resume daily supervised dispensing. Consider consult with addiction physician.
Presence of opioids or benzodiazepines	Innocent slip Early relapse	If inadvertent, warn patients not to take meds from family or friends. Increase testing frequency. If relapse: • Assess adequacy of buprenorphine/naloxone dose. • Counsel about avoiding triggers. • Assess mood. • Increase testing frequency. • If persists, reduce number of take-home doses.
Presence of cocaine or crystal methamphetamine	Possible stimulant use disorder	Consider consult with addiction physician

Indications for buprenorphine/naloxone tapering

- Patient wants to taper.
- Patient has at least six months without any substance use.
- Patient is socially stable and has a supportive family or social network.
- Patient has a stable mood and good coping strategies.
- Patient has minimal contact with drug users.

Buprenorphine/naloxone tapering protocol

- Decrease by small amounts, e.g., 2 mg or even 1 mg (half of a 2 mg tablet) at a time.
- Leave at least two weeks, preferably longer, between dose decreases.
- Put the taper on hold at the patient's request, or if the patient experiences withdrawal symptoms or cravings.
- Return to the original dose if the patient begins using opioids again, even in small amounts or intermittently.
- Provide regular support and encouragement.
- Emphasize that it is not a "failure" if the taper has to be held or reversed, and it is safe and acceptable to remain on buprenorphine/naloxone for long periods when necessary.

Part IV: Tobacco

Introduction

Cigarette smoking has an enormous cost for the Canadian population both financially and medically. In 2002, tobacco was responsible for 37,209 deaths, 515,607 potential years of life lost, and over $4.3 billion in direct health care costs in Canada (63). Although the percentage of Canadians who are current (daily or occasional) smokers has decreased from 25% in 1999 to 16% in 2012 (64), the health risks for these individuals are many and potentially life-threatening. Primary care providers can make a significant difference to patients' health outcomes by helping them decrease or stop their tobacco use. The Tobacco Use and Dependence Guideline Panel suggests the following model for smoking cessation (65):

The 5A's for smoking cessation

1. **Ask** about tobacco use.
2. **Advise** to quit.
3. **Assess** willingness to make a quit attempt.
4. **Assist** in quit attempt.
5. **Arrange** follow-up.

This section outlines the brief primary care interventions promoted by the Tobacco Use and Dependence Guideline Panel for screening, assessing, and treating patients' tobacco use.

Ask about tobacco use

- Ask all patients about their tobacco use.
- Ask patients if they smoke **currently** and if they have **ever** smoked.
- Keep track of each patient's smoking status.

Advise to quit

For all patients who smoke:

- Review the **health risks** of smoking (e.g., cardiovascular, oral, reproductive, cancer).
- Review **other harms** of smoking (financial, social, etc.).
- Link smoking to patient's own health condition if possible.
- Inform the patient that quitting smoking would be the **best thing they can do for their health**.
- Inform the patient that **you can help them quit** if they are interested in trying.

Assess willingness to make a quit attempt (66)

State of change (67)

"When would you be willing to consider quitting smoking?"

Never/6+ months	**Pre-contemplation** Ask how patient feels about smoking (without judgment). Follow up at subsequent visits.
1–6 months	**Contemplation** Explore patient's motivation to quit. Explore what patient gets out of smoking and consider alternatives. Inform patient about treatment options. Offer assistance. Follow up at subsequent visits.
< 1 month	**Preparation** Offer assistance. Set quit date. Review treatment options. Recommend smaller goal before quit date: stop smoking in certain settings (e.g., the car, evenings). Follow up within 2 weeks.
Now	**Action** Assist in quit attempt (see below) Arrange follow-up within a week to review progress.

Assist in quit attempt

Creating a quit plan (65)

- Work with patient to prepare to quit:
  - Set a firm quit date, ideally within the next two weeks.
  - Tell family and friends in order to increase accountability and ask for support.
  - Prepare for challenges that will arise early in the quit attempt and come up with solutions.
  - Create a tobacco-free environment.
- Review pharmacotherapy and psychosocial treatment options.
  - Combination of pharmacotherapy and counselling has been found to be most effective (65, 68); patients should be offered both whenever possible.

Pharmacotherapy

- Three medication options: nicotine replacement therapy (NRT), buproprion SP, varenicline.
- Numerous clinical trials and meta-analyses have shown that all three medications are superior to placebo in promoting smoking abstinence (69-71).
- An internet survey of users' preferences found that varenicline was preferred by patients who tried all three medications (72).
- Patients' preferences should be taken into account when selecting a medication.

1. NRT (73)

Action

- Relieves nicotine withdrawal symptoms and reduces harms caused by inhalation.
- Five formulations: gum, lozenge, patch, inhaler, nasal spray.
- Choice of formulation depends on patient's preference.

Side effects

- *Gum:* Bad taste, tingling sensation, hiccups, nausea, jaw pain.
- *Lozenge:* Nausea, hiccups, headache, heartburn, flatulence.
- *Patch:* Skin rash, sleep disturbances.
- *Inhaler:* Cough, throat irritation, nausea.
- *Nasal spray:* Nausea, tingling sensation, hiccups, dry mouth, heartburn, hiccups.

Contraindications and precautions

- Use caution in patients who have acute cardiovascular disease, are pregnant/breastfeeding, or are under 18 years old.

Dose

- Depends on formulation and number of cigarettes smoked per day.
- Titrate to effect.

2. Buproprion SR (74, 75)

Action

- Inhibits dopamine reuptake following lowering of nicotine intake.
- Weak noradrenalin reuptake inhibitor.

Side effects

- Agitation, insomnia, headache, dry mouth, rash, nausea, dizziness.
- Similar to nicotine withdrawal symptoms.

Contraindications and precautions

- History of seizure.
- Bipolar disorder.
- Eating disorder.
- Pregnancy or breast-feeding.
- Use caution in patients who are elderly, have liver/renal deficiencies, or are on medications that lower seizure threshold.

Dose

- 150 mg PO OD x 3 days; then 150 PO bid for 7–12 weeks.
- Patient should stop smoking during the second week of taking the medication.

3. Varenicline (76)

Action

- Nicotinic receptor partial agonist.

Side effects

- Nausea, headache, insomnia, sleep disturbances.
- Severe psychiatric events have been experienced by some patients taking varenicline; however, there is no conclusive evidence that these events were caused by the drug.

Contraindications and precautions

- Use caution in patients who are pregnant/breastfeeding or who have severe renal dysfunction.

Dose

- 0.5 mg PO OD x 3 days; 0.5 mg PO bid x 4 days.
- Patient should stop smoking on day 8 and increase dose to 1 mg PO bid for 12 weeks.

Counselling (65)

- Encourage patient to identify situations that increase risk of smoking (e.g., stress, being around smokers).
- Strategize about ways to cope with triggers:
  - Avoid situations that could lead to smoking.
  - Make lifestyle changes that reduce stress.
  - Make a list of activities for patient to do when struggling with a craving (e.g., go for a walk, listen to music, call a supportive friend, etc.).
  - Make a list of supportive people to call when triggered.
- Engage patient in quitting process by asking about positive benefits gained, milestones, and challenges.
- Remind patient that a setback does not need to become a relapse.
- Offer support and encouragement throughout process.

Arrange follow-up

- See patient frequently during quitting process:
  - Monitor medications.
  - Engage patient in counselling.
  - Acknowledge victories and discuss setbacks.
  - Provide support and accountability.
- Encourage participation in support groups or other forms of psychosocial treatment:
  - *Smokers' Helpline*: Phone support through the Canadian Cancer Society (1-877-513-5333)
  - Group and individual counselling sessions
  - Self-help

Part V: Cannabis

Introduction

Cannabis is the most widely used illicit substance worldwide. In Canada, cannabis is second only to alcohol as the most widely used psychoactive substance. Among adolescents, Canadian teens have the highest use of cannabis, with more than 20% reporting use in the past year, compared to 10% in other developed countries (77). There has been an increase in cannabis use disorder in the United States over the last ten years, especially in states where cannabis use has been decriminalized (78). It is estimated that 9% of people who use marijuana will become dependent on it at some point in their lives (77).

An additional factor is the Health Canada regulation allowing health care providers to authorize the use of cannabis for medical purposes. This, combined with the high number of users, the risk of dependency, and the possible legislative changes that may be on the horizon in Canada, makes it crucial for primary care providers to be able to communicate with their patients about cannabis. This section outlines the essentials of managing patients' cannabis use, both medical and recreational.

Harms associated with cannabis use

Route of delivery

- Smoking is most common route.
  - Smoking creates hundreds of chemical by-products, some of which are carcinogenic and atherogenic.
- Vaporizing avoids the toxic byproducts of smoking.
- With both smoking and vaporizing, THC rapidly enters the CNS in high concentrations, increasing the risk of cognitive impairment.
- THC absorption is slow with the oral route, but food products sometimes contain large amounts of THC, which can cause severe intoxication.

Long-term effects and complications

- Cognitive impairment
  - Can impact impulse control, working memory, decision-making, executive function (79)
- Psychiatric
  - Can trigger and exacerbate psychosis (80)
  - Cannabis use disorder (81)
  - Association between cannabis use and anxiety and mood disorders, though directionality is not entirely clear (82)
  - Risks greater under the age of 25

- Cannabis hyperemesis syndrome (83)
  - Difficult to diagnose, but often characterized by long-term cannabis use, cyclical vomiting, and a compulsive need for hot bathing
  - Can also be accompanied by reduced oral intake, abdominal pain, weight loss, dehydration
  - Condition resolves within 1–3 months of cannabis cessation; a return to cannabis can lead to recurrence
- Respiratory
  - Chronic bronchitis
  - Possible risk factor for lung cancer
- Cardiac
  - Tachyarrhythmias
  - Very high doses can precipitate myocardial infarction
- Reproductive
  - Neurodevelopmental delays in infants of women who use cannabis during pregnancy

Cannabis use during adolescence

- Canadian adolescents (age 11–15) have highest rate of cannabis use among 29 most developed countries (84).
- French study showed that a positive first exposure to cannabis may increase risk of developing cannabis dependence at age 18–21 (85).
- Other risks of cannabis use during adolescence:
  - Increase in social dysfunction (86).
  - Vulnerability of the adolescent brain to regular cannabis exposure (drop in IQ by 5–8 points) with changes persisting into midlife even after cessation (87, 88).
  - Heavy use may increase risk for developing psychosis (89).

Cannabis use and driving

- Cannabis use impairs performance of cognitive and motor tasks that are necessary for driving safely.
- Use of cannabis increases risk of a motor vehicle collision, with the risk increasing with driving after cannabis use and with using more than once weekly (90, 91).
- A meta-analysis of studies that looked at acute cannabis use and motor vehicle collisions found an almost doubling of risk for drivers involved in a collision that resulted in serious injury or death (92).
- Inform your patients that you have a duty to report to the Ministry of Transportation if you have concerns about safety and driving.
- Criteria for reporting to the Ministry of Transportation:
  - Patient or family member reports that patient is using cannabis before driving.
  - Patient reports that they are using cannabis throughout the day and also reports that they are driving.

Screening and assessment

Drug history

- Ask all adolescent and adult patients at baseline and annual physical about their use of all recreational substances, including cannabis.
- Ask about weekly **frequency** of cannabis use and typical **amount** they use in a day.
    - An average joint contains about 500 mg of dried cannabis; an average bowl contains about 250 mg of dried cannabis.
    - If patient is not sure how much they smoke in a week, ask them how much they purchase at a time and how long it takes them to go through it.
- Patients who use cannabis more than **3 times per week** or use more than **2 g per day** should have further assessment.

Screening questionnaire

- The CAGE-AID (CAGE Adapted to Include Drugs) questionnaire has been validated as a screening tool for substance use disorders (93).
- CAGE-AID is well suited to use in primary care, as it is quick and can be easily incorporated into a medical history or office visit.
- A score of 1+ indicates a need for further evaluation for cannabis use disorder (CUD).

CAGE-AID

In the last three months…

- Have you felt you ought to **C**UT DOWN or stop drinking or using drugs?
- Has anyone **A**NNOYED you or gotten on your nerves by telling you to cut down or stop drinking or using drugs?
- Have you felt **G**UILTY or bad about how much you drink or use drugs?
- Have you been waking up wanting to have an alcoholic drink or use drugs (**E**YE-OPENER)?

Managing cannabis use

Patients in certain risk categories should be discouraged from using cannabis regularly, whether or not they are identified has having a cannabis use disorder. Other patients who are not identified as having a cannabis use disorder should be given advice on harm reduction and reducing their use.

Discourage regular use

The following patients should be strongly discouraged from engaging in regular cannabis use:

- Patients under the age of 25.
- Patients who are pregnant or trying to become pregnant.
- Patients with a current, past, or strong family history of psychosis.
- Patients with a current, past, or strong family history of problematic substance use.
- Patients with a current anxiety or mood disorder.
- Patients with a respiratory or cardiac illness.

Advice on reducing cannabis use and avoiding cannabis-related harms

- Do not combine cannabis with alcohol or opioids.
- Do not drive for at least 6 hours after using (or at least 8 hours if you experience a subjective high).
- Use a vaporizer rather than smoking.
- Use very small amounts of edibles, as they can contain large amounts of THC.
- Abstain from cannabis at least 2 days per week.
- Set a weekly goal for cannabis use and keep a daily record of the amount used.
- Purchase smaller amounts and make smaller joints.
- Wait 10 minutes between puffs and 20–30 minutes between joints.
- Do not inhale deeply or hold your breath.

Cannabis use disorder

Patients scoring 1+ on the CAGE-AID screening questionnaire should be assessed for cannabis use disorder (CUD).

Diagnostic criteria

The DSM-V gives the following criteria for a CUD (17):

(a) Cannabis taken in larger amounts or over a longer period of time than intended.
(b) Repeated unsuccessful efforts to reduce use.
(c) Great deal of time spent obtaining or using cannabis, or recovering from its effects.
(d) Strong cravings or urges to use cannabis.
(e) Recurrent use resulting in a failure to fulfill major responsibilities.

(f) Continued cannabis use despite recurrent social or interpersonal problems.
(g) Reduction of major activities because of cannabis use (e.g., missing work, spending less time with children or spouse).
(h) Continued cannabis use in situations or activities where it is dangerous.
(i) Continued use despite knowledge of cannabis-related physical or psychological problems.
(j) Tolerance (need to use more cannabis to achieve the same effect, or diminished effects with continued use of the same amount of cannabis).
(k) Withdrawal (e.g., irritability, anxiety, sleep difficulty, decreased appetite, abdominal pain, sweating, headache, relieved by drinking).

Patients who meet two or three of these criteria have a **mild** CUD, four to five criteria indicate a **moderate** CUD, and six or more indicate a **severe** CUD.

Clinical features of CUD

- Baseline risk factors: younger, current psychiatric disorder, current or past problematic use of alcohol or other substances
- Smokes cannabis daily in large doses (e.g., 2–3+ grams)
- Spends a significant amount of time smoking every day
- Poor psychosocial function (family, work, school)
- Strong resistance to discontinuing cannabis
- Believes that cannabis is essential to relieve anxiety
- Concern expressed by family members

Patient intervention

- Tell patient that you believe that their cannabis use is harmful to them.
- Explain that, while cannabis intoxication may temporarily relieve anxiety, in the long term it makes mood worse, and mood, function, and relationships will improve if cannabis use is reduced or stopped.
- Use a motivational interviewing approach with patients who are ambivalent about treatment (94):
  - Explore patient's own reasons for change with the goal of encouraging **change talk**.
  - Ask: "What are some of the good things about using cannabis? What are some of the not-so-good things? How does using cannabis fit in with your goals? What are some of the good things about **not** using cannabis? What are some of the not-so-good things? How would you like your life to be different? Where do you go from here?"
  - Reflect back patient's motivations in order to strengthen commitment to change.
  - Non-confrontational, patient-centred approach that elicits higher levels of change talk and lower levels of resistance in patients than other approaches.
- Ask if patient is willing to commit to a goal (abstinence or reduced use).
- If patient is not ready to commit, ask about cannabis use and readiness to change at each visit.
- If ready to commit, negotiate a goal:
  - If reduced use is chosen, offer advice on reducing use and harms (see page 89).
- Treat concurrent mood or anxiety disorders.

- Encourage healthy lifestyle choices:
  - Work with your clinician to quit tobacco (if applicable).
  - Avoid friends who use cannabis regularly.
  - Avoid social situations involving cannabis use.
  - Find alternative activities, such as exercise and spending time with friends.
  - Find someone you can talk to about your cannabis use.
- Offer pharmacotherapy to treat withdrawal symptoms and cravings:
  - Some preliminary evidence for nabilone, gabapentin, and over-the-counter N-acetylcysteine (NAC) (95).
  - Nabilone: Starting dose **1 mg tid**; titrate to effect
  - Gabapentin: 1200 mg daily
  - NAC: 1200 mg daily
- Refer to psychosocial treatment if available.
- Arrange regular follow-up to discuss progress.
- Perform urine drug screens in follow-up visits to encourage patient accountability and monitor cannabis use (96).
  - A single use can produce a positive urine drug screen up to 1 week after use.
  - Long-term users can have positive urine drug screens up to 46 days after last use.

Cannabis withdrawal

- Onset: Several days after daily heavy use
- Symptoms: Anxiety, irritability, depression, insomnia, abdominal discomfort, sweating, headache

Cannabis therapy

Health Canada allows health care providers to authorize the use of cannabis for medical purposes for their patients; however, cannabis is **not** an approved therapeutic product in Canada, nor has any medical regulator endorsed or approved cannabis as a safe and effective therapy. This means that, in the event that a patient experiences harm from medical cannabis, the authorizer cannot claim that they were prescribing according to approved medical standards. Primary care providers receiving requests for cannabis authorization should keep the following guidelines in mind:

- Health care providers are not obligated to authorize cannabis.
- Health care providers should monitor all patients on cannabis therapy for indications of harm, including misuse.
- Health care providers should stop authorizing cannabis to patients when there is evidence of harm.

Although Health Canada regulations allow the sale of dried cannabis, fresh cannabis, and cannabis products (e.g., oils), the only clinical trials on the therapeutic effect of cannabinoids have involved inhaled cannabis and synthetic products (e.g., nabilone); as well, inhaling remains the most common delivery route, and dried cannabis is the most widely available product from Canadian licensed producers. This section will therefore focus exclusively on medical authorization for the consumption of dried cannabis.

Evidence for cannabis therapy for pain

- Evidence very weak (97):
  - Five placebo-controlled RCTs on subjects with neuropathic pain.
  - Trial durations ranged from 1–5 days, total of 226 subjects.
  - Functional outcomes not assessed.
  - Subjects in cannabis group experienced dose-dependent cognitive impairment and intoxication.
- Nabilone (oral pharmaceutical cannabinoid) and nabiximols (buccal THC/cannabidiol spray) both have greater evidence of safety and effectiveness for pain than dried cannabis (98).

Evidence for cannabis therapy for anxiety

- Observational studies have shown that cannabis use worsens anxiety and PTSD symptoms; stopping cannabis use improves anxiety and PTSD symptoms (99, 100).
- Pure cannabidiol (with no THC) may have some therapeutic benefit in treating anxiety (101).

Evidence for cannabis therapy for nausea

- Small review of state clinical trials (102) showed that smoked cannabis has some benefit in reducing chemotherapy-related nausea and vomiting. However, these trials are of varying quality, with some results consisting entirely of patient satisfaction.
- Systematic review (103) found that synthetic cannabinoids have a slightly better antiemetic effect in patients with cancer than conventional antiemetics, but also have more side effects.

Evidence for cannabis therapy for epilepsy

- A recent RCT (104) found that synthetic cannabidiol reduced the frequency of seizures in children and adolescents with drug-resistant Dravet syndrome (a form of epileptic encephalopathy), although it was also associated with adverse events.

Indications

- Severe neuropathic pain condition (e.g., HIV, diabetes) that has failed to respond to an adequate trial of all standard analgesics (opioids, anticonvulsants, antidepressants, pharmaceutical cannabinoids).
- Not indicated for fibromyalgia, low back pain, or other common pain conditions seen in primary care.
- Not indicated for anxiety, PTSD, insomnia, or depression.

Contraindications and precautions

- Age under 25
- Current, past, or strong family history of psychosis (80)
- Cardiovascular or respiratory disease
- Current, past, or strong family history of problematic substance use (alcohol, opioids, benzodiazepines, stimulants)
- Current, active mental illness (anxiety, depression, PTSD)
- Pregnant or planning to get pregnant

Authorizing cannabis therapy

Dosing

- Authorizers must complete a medical document specifying the daily amount of dried cannabis and the period of use (maximum one year).
- No legal restriction on the amount of cannabis authorized.
- Possession limit: the lesser of the equivalent of 150 g or 30 times the daily amount authorized.
- While not legally required, authorizers should also specify the THC and cannabidiol concentrations.
- Maximum recommended daily dose of dried cannabis: **400 mg with maximum 9% THC**
  - Maximum dose used in controlled trials (105)
  - Recommended by College of Family Physicians of Canada guidance document (106)
- Acute and long-term adverse effects are related to the dose of THC:
  - Cannabidiol may mitigate against the harmful psychoactive effects of THC.
  - Prescriptions should specify a cannabidiol concentration at least as great as THC.

Management of requests for dried cannabis

- If dried cannabis is not indicated or contraindicated:
  - Explain that standard treatments are safer and more effective.
  - Explain that dried cannabis carries serious risk of harm, especially in higher doses, when it is contraindicated.
  - Assess patient for a cannabis use disorder, especially if patient is persistent or aggressive.

Medical cannabis clinics

- Use **caution** when referring patients to medical cannabis clinics.
- Some clinics authorize excessive amounts of cannabis (e.g., 2–3 g per day) for non-indicated conditions for patients at high risk for cannabis-related harms.
- Do not refer to medical cannabis clinics unless they have released a **detailed clinical summary** of their authorizing practices (assessment, indications, contraindications, dosing, and monitoring).

Part VI: Benzodiazepines

Introduction

Benzodiazepines are effective anxiolytics, but they are associated with serious harms. Health care providers find it difficult to mitigate against these harms because they tend to be unpredictable, vague and hard to detect, and multifactorial (e.g., falls, fatigue, depression). Therefore, as with opioids, safe benzodiazepine prescribing requires careful patient selection, close monitoring, and tapering when indicated. This section provides guidelines on safely prescribing benzodiazepines and managing adverse effects, including benzodiazepine use disorder.

Benzodiazepine therapy

Indications

- Severe acute anxiety
- Generalized anxiety disorder that is unresponsive to other treatments (e.g., SSRIs, SNRIs)
- Panic disorder that is unresponsive to other treatments (SSRIs are first-line agents)
- Depression, bipolar disorder, or schizophrenia (adjunct therapy)
- Insomnia
- Alcohol withdrawal
- Seizures, spasms
- Pre-procedure sedation

Adverse effects

Effect	Factors that increase risk
Depression Suicidal ideation	• High doses • Concurrent use of alcohol/opioids • Underlying mood disorder
Falls Hip fractures	• Older adults • Neurological/cognitive impairment • Long-acting agents (e.g., diazepam)
Confusion Worsening dementia	• Older adults • Dementing condition
Motor vehicle accidents	• Early in therapy before tolerance develops • Concurrent use of other sedating agents
Decreased respiratory drive	• Early in therapy • Respiratory illness/dysfunction • Concurrent use of other sedating agents
Sleep apnea	• Underlying risk (e.g., obesity) • Concurrent use of other sedating agents
Blackouts Parasomnias	• Triazolam or alprazolam • Higher doses

Prescribing benzodiazepines

- Consider alternative therapies before prescribing benzodiazepines.
  - For anxiety: SSRIs, SNRIs, mood stabilizers, psychotherapy
  - For insomnia: trazadone, tryptophan, low-dose TCA, sedating SSRIs, zopiclone
- Initial prescriptions should be for a maximum of **3 weeks**.
- Prescribing for anxiety:
  - Titrate patient to lowest effective dose.
  - Long-term therapy should be prescribed only to patients with severe anxiety interfering with daily function who have failed an adequate trial of psychotherapy and of other anxiolytics (e.g., SSRIs, mood stabilizers).
  - Taper dose when indicated (see below).
- Prescribing for insomnia:
  - Patients should avoid daily use for prolonged periods, as tolerance for sedation develops quickly, and abruptly stopping after several weeks of daily use will result in rebound insomnia.
  - Patients should be advised on sleep hygiene:

Go to bed and get up at a reasonable time; don't sleep late, even if you're tired.
Eat only small amounts before bed.
Avoid caffeine and alcohol at night.
Only use the bed for sleeping and sex; don't read, watch TV, use your phone, etc.
If you can't sleep, get up and do something else for 15 minutes (but don't turn on a screen).
Exercise most days of the week.
If you get up frequently to urinate, avoid drinking too much at night.

Benzodiazepine equivalent table (107)

Benzodiazepine	Equivalent to 5 mg diazepam*
Alprazolam**	0.5 mg
Bromazepam	3–6 mg
Chlordiazepoxide	10–25 mg
Clonazepam	0.5–1 mg
Clorazepate	7.5 mg
Flurazepam	15 mg
Lorazepam	0.5–1 mg
Nitrazepam	5–10 mg
Oxazepam	15 mg
Temazepam	10–15 mg
Triazolam**	0.25 mg

* Equivalences are approximate. Careful monitoring is required to avoid over-sedation, particularly in older adults and those with impaired hepatic metabolism.

** Equivalency uncertain.

Benzodiazepine withdrawal

Clinical features	Abrupt discontinuation of benzodiazepines after daily use for 2+ months Can occur even at therapeutic doses, though more severe with high doses, long duration of use, or underlying anxiety disorder
Time course	Onset 2–4 days after abrupt cessation May take weeks or months to resolve
Symptoms and signs	Anxiety-related symptoms (panic, irritability, poor concentration) Neurological symptoms (dysperceptions, tinnitus, déjà vu) Sweating, tremor usually not seen except with sudden cessation of high doses
Complications	Abrupt cessation of high doses (50 mg of diazepam/day or equivalent) can cause acute hypertension, seizures, delirium Can trigger suicidal ideation in patients with mixed anxiety and mood disorder
Effect on sleep	Rebound insomnia (vivid dreams, fitful sleep) Takes several weeks to resolve

Benzodiazepine tapering

Rationale

- Recommended over abrupt cessation unless patient has only been taking the medication intermittently or for a few weeks.
- Periodic tapering attempts are warranted even for patients taking therapeutic doses with no apparent adverse effects:
  - Patients sometimes feel more alert and energetic at lower doses, and are better able to engage in psychotherapy.
- Controlled trials have shown that many adults are able to successfully reduce their benzodiazepine dose with appropriate support (108, 109) and that tapering can be performed in primary care (110).

Indications

- At higher risk for sedation, falls, and sleep apnea (e.g., elderly, heavy drinkers, on opioids or other sedating medications)
  - Benzodiazepines markedly increase opioid toxicity and the lethality of an opioid overdose (111).
- Daily responsibilities requiring alertness and clear thinking (e.g., students, drivers, looking after small children)
- Cognitive impairment, fatigue, depression
- At risk for unsafe medication use

Approach to tapering

- Explain benefits of tapering (improved energy, mood, and function; reduced risk of falls; etc.).
- Work with patient to determine rate of taper.
  - Slow, flexible tapers work better than rapid tapers.
- Halt or reverse taper if patient experiences clinically significant increase in anxiety.
- Follow patient regularly (every 1–4 weeks).
- At each visit, ask not just about withdrawal symptoms but benefits of tapering: more alert, less fatigued, improved mood.
- Involve family members if possible; they often notice improvement before patient does.
- Ideal time to introduce comprehensive management strategies for underlying anxiety disorder, including psychotherapeutic techniques (mindfulness, CBT), lifestyle modification (exercise, sleep, reduce coffee and alcohol) and pharmacotherapy (antidepressants).

Tapering protocol

Formulation	Safest to taper with patient's current benzodiazepine (but see below).
Dosing interval	Scheduled doses rather than PRN. Keep dosing interval the same for as long as possible (e.g., bid or tid). Advise patients not to skip or delay doses (in an attempt to speed up the taper), as this causes a sharp increase in anxiety.
Rate of taper	Taper slowly, no more than 5 mg diazepam equivalent/day at each office visit. Can taper as slowly as 1–2 mg diazepam equivalent/month. Can taper according to proportional dose remaining: taper by 10% of dose every visit until at 20% of original dose, then taper by 5% every visit. Let patient choose which dose is decreased (AM, PM, or HS). Adjust rate of taper according to patient response. Slow pace of taper once daily dose below 20 mg diazepam equivalent.
Dispensing interval	If patient runs out early, increase dispensing frequency to weekly, alternate days, or daily.
Endpoint of taper	Abstinence preferred. Reduced dose if patient experiences significant anxiety or insomnia with abstinence.

Tapering with clonazepam

- If patient is emotionally attached to their benzodiazepine and resistant to tapering or repeatedly runs out early, consider switching patient to another agent for tapering.
- Little clear evidence for best agent for tapering; however, **clonazepam** is recommended over diazepam.
  - Although diazepam has a longer duration of action and therefore may result in a smoother withdrawal, clonazepam is less likely to cause prolonged sedation in the elderly and has a lower risk of euphoria and misuse.
- Protocol:
  - Initial dose should be lower than that of current agent, as patient may not be tolerant to new agent; convert to one half equivalent dose of original agent.
  - Increase dose until patient is comfortable, but try not to go above fully equivalent dose.
  - Prescribe on bid or tid schedule.

Benzodiazepine use disorders

As with opioid use disorders, a patient with a benzodiazepine use disorder is not using the medication for therapeutic purposes but to achieve sedation and euphoria. While tolerance for the anxiolytic effects of benzodiazepines develops very slowly, allowing patients to stay on a moderate dose for months or years, tolerance to the sedating and euphoric effects of benzodiazepines develops quickly, forcing patients to escalate the dose. The features of benzodiazepine **intoxication** are similar to those of alcohol intoxication: sedation, emotional lability, and impulsive or dangerous behaviour.

Risk factors

- Male
- Younger
- Current or past history of problematic use of other substances
- Current active psychiatric disorder

Clinical features

- Patient is taking a dose well above the usual therapeutic range.
- Patient frequently runs out early or accesses benzodiazepines from other sources.
- Patient has a pattern of binge use with recurrent intoxication and withdrawal.

Management

Treatment setting	Outpatient taper recommended for patients on moderate doses who do not access benzodiazepines from non-medical sources. Residential treatment best for patients on very high doses (e.g., 100+ mg diazepam equivalent/day) or patients whose main source of benzodiazepines is the illicit market.
Outpatient tapering	Patients will have trouble tapering if they are given large amounts of benzodiazepines to take home. Dispense every 1–2 days with a strict agreement that prescriptions will not be refilled early. Patients experiencing significant sedation or intoxication should be tapered quickly (e.g., 5 mg diazepam equivalent every 3–7 days). Taper may be slowed when intoxication resolves.
Psychosocial treatment	Similar to treatment of other substance use disorders: formal treatment programs and self-help groups. Encourage patient to try different options to see what suits them best.
Treatment of concurrent conditions	Addiction to alcohol or opioids should be treated at the same time as the benzodiazepine addiction to reduce risk of dangerous drug interactions. Most patients with a benzodiazepine use disorder will also have a significant mental illness, which should be treated concurrently. Anticonvulsant medications (e.g., gabapentin, topiramate) may be helpful for both underlying mood disorder and alcohol/benzodiazepine withdrawal. Antidepressants and atypical antipsychotics may also be helpful. Shared care with psychiatrist is recommended.

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