

**Management of alcohol use
disorders, opioid
prescribing, and opioid use
disorders in primary care:
A pocket reference for
family physicians**

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Part I: Alcohol use disorders

Introduction

Until recently, primary care physicians' 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 (1); there is evidence that the length of treatment has a greater impact on outcome than the intensity of treatment (2). 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 (3-6). However, despite compelling evidence for physician involvement with alcohol use disorders, physicians do not consistently screen for alcohol or drug problems, counsel their addicted patients, or refer patients to formal treatment (7). 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 (8):

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 (9):

- (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 (10-12), binge drinking question (13), AUDIT (14).
- 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 **CUT DOWN** on your drinking?
Have people **ANNOYED** you by criticizing your drinking?
Have you ever felt bad or **GUILTY** about your drinking?
Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover (**EYE-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)

<i>1. How often do you have a drink containing alcohol?</i>				
0 Never	1 Monthly or less	2 2–4 times per month	3 2–3 times per week	4 4+ times per week
<i>2. How many drinks containing alcohol do you have on a typical day when you are drinking?</i>				
0 1–2	1 3–4	2 5–6	3 7–9	4 10+
<i>3. How often do you have 6 or more drinks on one occasion?</i>				
0 Never	1 Less than monthly	2 Monthly	3 Weekly	4 Daily or almost daily
<i>4. How often during the last year have you found that you were not able to stop drinking once you had started?</i>				
0 Never	1 Less than monthly	2 Monthly	3 Weekly	4 Daily or almost daily
<i>5. How often during the last year have you failed to do what was expected of you because of drinking?</i>				
0 Never	1 Less than monthly	2 Monthly	3 Weekly	4 Daily or almost daily
<i>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?</i>				
0 Never	1 Less than monthly	2 Monthly	3 Weekly	4 Daily or almost daily
<i>7. How often during the last year have you had a feeling of guilt/remorse after drinking?</i>				
0 Never	1 Less than monthly	2 Monthly	3 Weekly	4 Daily or almost daily
<i>8. How often during the last year have you been unable to remember what happened the night before because you had been drinking?</i>				
0 Never	1 Less than monthly	2 Monthly	3 Weekly	4 Daily or almost daily
<i>9. Have you or someone else been injured because of your drinking?</i>				
0 No	2 Yes, but not in the past year		4 Within the past year	
<i>10. Has a relative, friend, doctor, or other health worker been concerned about your drinking or suggested that you cut down?</i>				
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 (15, 16).

GGT	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Recurrent • Not related to sports activities • Occurs during/after social event
GI	Gastritis and esophagitis	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Not explained by other conditions (obesity, diabetes, viral hepatitis, medication use)
Cardio-vascular	Hypertension	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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 physician 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 (17, 18)

- 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, acamprostate, 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 the Connex DART database or 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 (19).
- 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 \geq 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. Sweating, Hallucination, Orientation, Tremor (SHOT) scale (20): Simple scale validated in the ED
2. Clinical Institute Withdrawal Assessment for Alcohol, Revised (CIWA-Ar) (21): Standard monitoring scale, strong evidence of validity

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 occasions 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.

Withdrawal severity scales

(1) 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.

(2) CIWA-Ar scale

<p>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</p>	<p>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</p>
<p>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</p>	<p>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</p>

<p>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.</p> <p>Observation 0 not present 1 very mild 2 mild 3 moderate 4 moderately severe 5 severe 6 very severe 7 extremely severe</p>	<p>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</p>	<p>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</p>
<p>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</p>	<p>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</p>	<p>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</p>

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

- For patients on Ontario Drug Benefits, the physician must apply to the Exceptional Access Program (EAP) to obtain coverage for naltrexone and acamprosate.
- 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 EAP approval.
- Disulfiram is only available in Canada as a compounded medication. The patient can ask his/her pharmacy to arrange for compounding.

Medications

1. Disulfiram (22-26)

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 (27)

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 (28, 29)

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 (30-32)

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 (33-35)

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 (36, 37)

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 (38)

- 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 (39)

Risk

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

Physical signs

- Spider nevi, 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 (40)

- 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 physician 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 II: Opioid prescribing and opioid use disorders

Introduction

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 (41, 42). Evidence suggests that physicians' prescribing practices are a major contributor to these harms. 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 (43). However, these guidelines have had little appreciable effect: many Ontario family physicians continue to overprescribe opioids, while some are extremely uncomfortable prescribing opioids at all. What follows outlines the role of opioids in CNCP management, provides a clear protocol for prescribing opioids, and advises on how to reduce, mitigate, or prevent the harms associated with chronic opioid use.

Initiating opioid therapy

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 imaging, 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 NSRIIs).
- Note: Opioids are not indicated for common pain conditions such as fibromyalgia, low back pain, and headaches.

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.
- 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, SNRIIs
 - Neuropathic pain: anticonvulsants, SNRIIs, 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.
- 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 preparations of codeine, tramadol (e.g., Tramacet[®], Ultram[®], Zytram XL[®]), or buprenorphine patch (BuTrans[®]). These medications are effective, and they have a much lower risk of overdose, addiction, sedation, and falls than the potent opioids.
- If insufficient analgesia with first-line opioids, prescribe morphine (various generics), oxycodone (various generics,

OxyNEO[®]), or hydromorphone (e.g., Dilaudid[®], Hydromorph Contin, Journista[®]).

- 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 (various generics, Duragesic[®]) 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 daily (MED) for at least 2 weeks.

Opioid initiation and dose titration

Opioid	Max initial dose*	Max dose increase	Min # of days between increases	Min IR dose before moving to 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**	IR 700 mg/d, CR***	100 mg/d CR	3 days CR	-----

* Starting dose is 40 mg MED (less for seniors).

** Potent opioids should only be dispensed to patients currently taking weak opioids daily. All dose increases should be based on an individual assessment.

*** CR: Start 50 mg bid in opioid-naïve, ≥50 mg bid if switching from other opioids. Maximum 250 mg bid. Exert caution when switching from pure mu-opioids.

Morphine equivalency

Opioid	Analgesic equivalence value
Morphine (reference)	30 mg
Codeine	200 mg
Oxycodone	20 mg
Hydromorphone	6 mg
Tapentadol	No equivalence to morphine established, but CR has demonstrated comparable pain relief to oxycodone CR (dose ratio 5:1)
Transdermal buprenorphine	No equivalence to morphine established
Transdermal fentanyl	25 µg/hr = 60–134 mg oral morphine per 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.

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 MED 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 90–120 mg MED, the physician should reassess the opioid’s analgesic effectiveness and side effects, and decide whether to maintain the dose or taper.

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.
- 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.

(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 doctor 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

- Increase fibre, fluid, and activity.
- If laxatives are needed, consider polyethylene glycol (Restorolax), sodium picosulphate (Dulcolax) or lactulose. Polyethylene glycol is most effective for opioid-induced constipation.

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 when a patient has failed at opioid therapy, tapering the dose improves pain, mood, and functioning.
- Tapering is a **far safer option** than abrupt cessation of opioid prescribing:
 - Abrupt cessation will trigger severe withdrawal, and patients will lose their opioid tolerance within days, creating a heightened risk of overdose.

Indications for opioid tapering

- The patient has persistent severe pain and pain-related disability despite an adequate opioid dose (e.g., 60 mg/d MED), and the patient has already failed on a trial of at least one opioid previously.
- The patient has a complication from opioid therapy, such as sleep apnea, sedation, or dysphoria.
- Part of structured opioid therapy for patients who have or are at high risk for an opioid use disorder.

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, no more than 10% of total daily dose every 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	≥ 60 mg MED (controls pain with minimal side effects).
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.

Opioid switching

Indications for opioid switching

- Inadequate analgesic response to the current opioid (< 2/10 pain relief, no improvement in function) despite a reasonable dose (e.g., 60 mg MED). 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.

Opioid switching protocol

- Because the patient will not be fully tolerant to the new opioid, its MED should be 50% of the MED of original.
- *Example:* When switching a patient from 40 mg/d of oxycodone to hydromorphone:
 - 40 mg/d oxycodone = 60 mg MED
 - 60 mg MED = 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 37.

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 (used patches contain a large amount of fentanyl, and patches can be easily lifted off the skin of a sleeping patient).
- Consider a fentanyl patch exchange program at the pharmacy (<http://www.patch4patch.ca>): patients place their used patch on a piece of paper so the pharmacist can make sure it has not been cut or manipulated.
- 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.

Monitoring for misuse

- Any patient with an ongoing opioid prescription of 40 mg MED or more should be monitored for signs of opioid misuse.
- At each visit, the physician should assess the patient for:
 - Changes in their mood, relationships, or functioning
 - Concerns expressed by family or close friends
 - Unauthorized changes to the dose, schedule (i.e., binge use), or route of delivery (i.e., biting oral tablets, etc.) of their medication
 - Euphoric effects (e.g., relaxation, confidence, energy) immediately after taking a dose
 - Withdrawal symptoms (see pages 48–49)
 - 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 (9):

- (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 physician 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

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; 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 but often preferred by patients. Patients are at increased risk for opioid overdose after leaving abstinence-based programs, so they should be given overdose prevention strategies:

- Never use opioids alone; always use with a friend and make sure you are both aware of the signs of overdose.
- If you are taking opioids after a period of abstinence of any length, take a much smaller dose than you used to.
- Do not inject opioids.
- Do not mix opioids with other substances, especially alcohol or benzodiazepines.
- Always carry naloxone.

(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 physician.
- 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 40).
- 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 or methadone treatment if structured opioid therapy fails (e.g., patient continues to access opioids from other sources).

(c) 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). While family physicians cannot prescribe methadone unless they have a special exemption from the CPSO, they can prescribe buprenorphine, which is now available as a General Benefit on the Ontario Drug Benefit Formulary.

Indications

- Has an OUD.
- Failed at or not a candidate for structured opioid therapy.
- Acquires opioids from multiple sources (e.g., other doctors, friends and relatives, the street).
- Injects or crushes oral tablets.
- Currently misusing alcohol or other drugs.

Prescribing buprenorphine

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

- Physician must ensure that patient has no opioid in their serum before taking the first dose.
 - Buprenorphine 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 again.
 - Use the Clinical Opioid Withdrawal Scale (COWS) to gauge the patient's withdrawal:

Clinical Opioid Withdrawal Scale (COWS) (44)

Date	Interval	0	30m	2h	4h
	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	Initials	Initials	Initials	Initials
> 36 SEVERE				

- **Give first dose in office setting, if feasible.**
 - 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.**
- **If office induction is not feasible:**
 - Give take-home prescription for 12 2 mg tablets.
 - Tell patient they must be in withdrawal before taking first dose; instruct them to wait at least 12 hours from last opioid use.
 - Take 2 mg x 2 tabs SL.
 - If still in withdrawal after 2 hours, take another 2 mg x 2 tabs SL. **Maximum dose first day is 8 mg.**
- 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 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 or other factors, then the physician should 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
- The physician should arrange frequent office visits for counseling and urine drug screen monitoring.

Buprenorphine 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.

Follow-up visits for stable patients on buprenorphine

- 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 meds used for mood control: <ul style="list-style-type: none"> • Assess adequacy of buprenorphine 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 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 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 for long periods when necessary.

Benzodiazepine tapering

Tapering rationale

- Benzodiazepines increase the risk and severity of opioid-induced fatigue, sedation, inattention and overdose.

Indications

- On multiple daily doses of benzodiazepines.
- In initiation/titration phase of opioid therapy or on a moderate to high opioid dose (> 60 mg MED).
- At high risk for opioid toxicity: elderly, impaired renal function, cognitively impaired, on other sedating drugs (e.g., atypical antipsychotics).
- At high risk for opioid use disorder (young, past or strong family history of addiction, current active psychiatric illness).
- Currently addicted to opioids (as part of structured opioid therapy).

Approach to tapering

Patient education	<ul style="list-style-type: none"> • Explain that tapering will improve mood and function and reduce the risk of adverse effects. • Patient will help the physician decide the rate of the taper; it will be slowed, halted, or reversed if the patient experiences difficulties.
Formulation	<ul style="list-style-type: none"> • Safest to taper with the patient's current benzodiazepine. • If switching to a different benzodiazepine, clonazepam is the preferred agent. Diazepam can cause prolonged sedation in the elderly and has a somewhat higher risk of euphoria and misuse than clonazepam.
Dosing interval	<ul style="list-style-type: none"> • Scheduled doses rather than PRN. • Keep dosing interval the same for as long as possible (BID or TID). • Advise patients not to skip or delay doses.
Rate of taper	<ul style="list-style-type: none"> • Taper slowly, no more than 5 mg diazepam equivalent/day at each office visit. • Can taper as slowly as 1–2 mg diazepam equivalent per month. • Let patient choose which dose is decreased (AM, PM, or HS). • Slower tapers are advised for patients who have been on benzodiazepines for a number of years, and patients with an underlying anxiety disorder.
Dispensing interval	<ul style="list-style-type: none"> • If patient runs out early, increase frequency to weekly, alternate days, or daily.
End point of taper	<ul style="list-style-type: none"> • Abstinence preferred. • Reduced dose if patient experiences significant anxiety or insomnia with abstinence.
Frequency of visits	<ul style="list-style-type: none"> • If possible, see patient prior to each dose decrease.
Approach at each visit	<ul style="list-style-type: none"> • Ask not just about withdrawal symptoms but benefits of tapering: more alert, less fatigued, improved mood. • Involve family members if possible; they often notice improvements before patient does.

Benzodiazepine equivalent table (45)

Benzodiazepine	Equivalent to 5 mg diazepam (mg)*
Alprazolam (Xanax®)**	0.5
Bromazepam (Lectopam®)	3–6
Chlordiazepoxide (Librium®)	10–25
Clonazepam (Rivotril®)	0.5–1
Clorazepate (Tranxene®)	7.5
Flurazepam (Dalmane®)	15
Lorazepam (Ativan®)	0.5–1
Nitrazepam (Mogadon®)	5–10
Oxazepam (Serax®)	15
Temazepam (Restoril®)	10–15
Triazolam (Halcion®)**	0.25

* 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

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
Effect on sleep	Rebound insomnia (vivid dreams, fitful sleep) Takes several weeks to resolve

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