Alcohol use disorder and withdrawal- how to help my patient in the clinic setting

Workshop Session- McGill Refresher Course 2022

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Disclosures

I have no disclosures to make

- I have worked with Abbvie and Gilead for Hepatitis C treatments for this patient population.
- I have worked with Indivior and participated in an advisory board for their products in May 2021.

Learning Objectives

Participants should be able to:

1. Be comfortable with the signs and symptoms of alcohol withdrawal.

2. Be able to assess an appropriate patient for outpatient withdrawal management.

3. Understand the management of outpatient alcohol withdrawal.

4. Follow long term relapse prevention for these patients.

Alcohol

- Alcohol is by far the most common drug used by Canadians
- 2017: **rate of hospitalizations** entirely caused by alcohol was comparable to the rate of hospitalization for heart attacks (249 vs 243 per 100,00) and the rate was thirteen times higher than for opioids
- 2014: alcohol represented **22% of all substance use attributable deaths** (14,826)

2014: $14,6 billion in **alcohol-related harms**

2017: among general population who consumed alcohol in the past 12 months, 20.8% (**16% of the total population**) exceeded the LRDGs for chronic effects, 14.8% for acute effects.

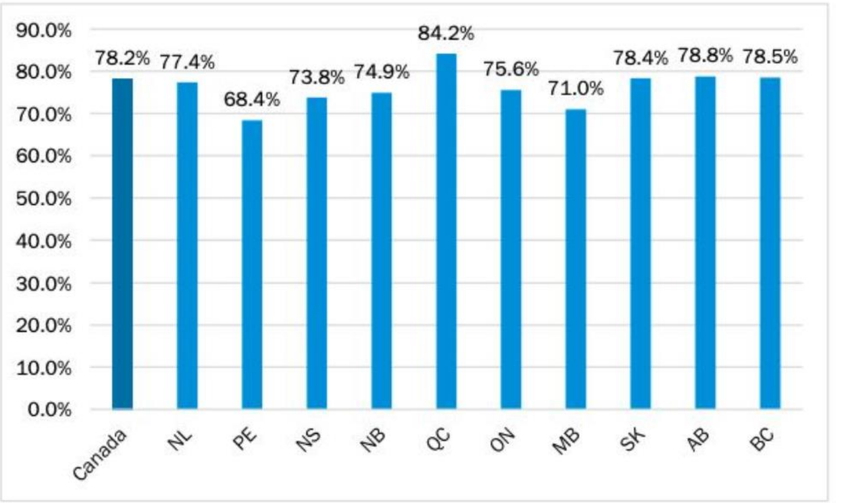
desired effects: euphoria, reduced inhibition, decreased anxiety, relaxation

side effects: slurred speech, sedation, dizziness, nausea, vomiting, diarrhea, urinary incontinence, muscular spasms, tremors, lack of coordination, general anesthesia, amnesia

overdose: seizures, hallucinations, decreased HR, hypotension, watering eyes, respiratory depression, unconsciousness, coma, death

withdrawal: tremor, diaphoresis, anxiety, agitation, confusion, delirium and psychosis

Figure 5: Prevalence of self-reported past-year alcohol use across provinces (2017)



https://www.canada.ca/en/health-canada/services/substance-use/alcohol/low-risk-alcohol-drinking-guidelines.html

Safe drinking guidelines for alcohol

Beer

341 ml (12 oz.)
5% alcohol content

Cider/cooler

341 ml (12 oz.)
5% alcohol content

Wine

142 ml (5 oz.)
12% alcohol content

Distilled alcohol
(rye, gin, rum, etc.)

43 ml (1.5 oz.)
40% alcohol content

The guidelines for consumption limits

Women:

- limit alcohol to no more than:
  - 2 standard drinks per day
  - 10 standard drinks per week
  - 3 standard drinks on special occasions
- avoid drinking alcohol on some days

Men:

- limit alcohol to no more than:
  - 3 standard drinks per day
  - 15 standard drinks per week
  - 4 standard drinks on special occasions
- avoid drinking alcohol on some days

https://www.canada.ca/en/health-canada/services/substance-use/alcohol/low-risk-alcohol-drinking-guidelines.html

Alcohol use- some statistics

Figure 1 **Crude rates for Hospitalizations Entirely Caused by Alcohol per 100,000 population age 10+, by age group and sex, 2015-2016**

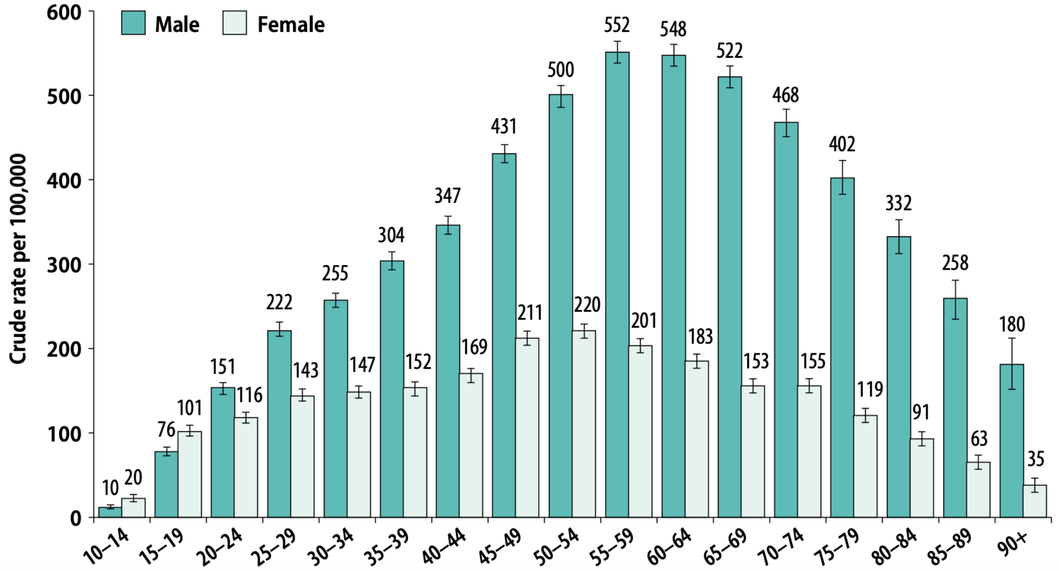
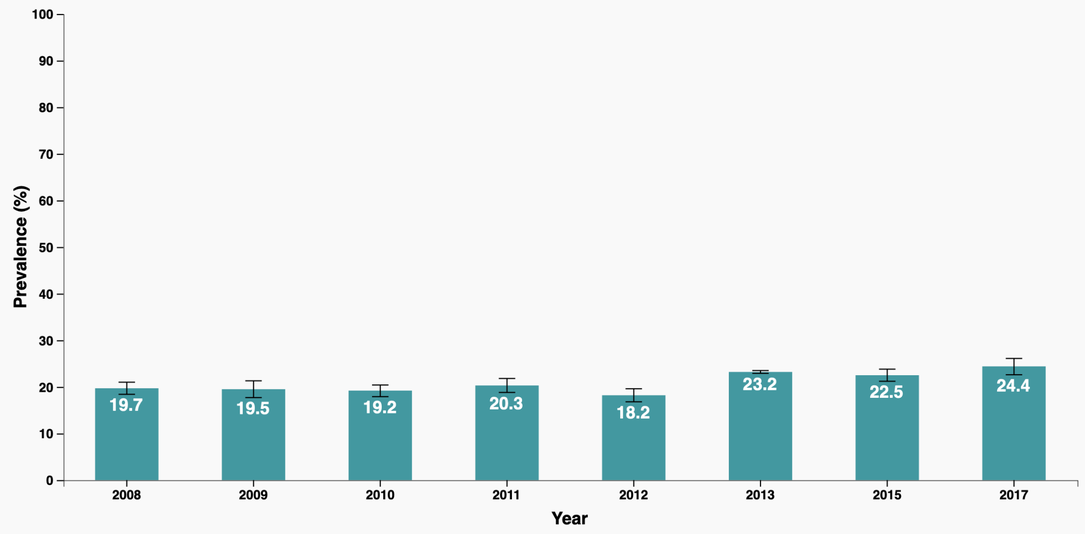


Figure 4. Prevalence (%) of past-12-month heavy drinking[1] among the general population, 15 years and older, Canada[2], 2008 to 2017



[1]Heavy drinking refers to males who reported having five or more drinks or females who reported having four or more drinks, on one occasion, at least once a month in the past year.

https://health-infobase.canada.ca/alcohol/ctads/

https://ccsmh.ca/wp-content/uploads/2019/12/Final_Alcohol_Use_DisorderV6.pdf

Alcohol use- some statistics

- **One in five Canadians** over the age of 15 years old meet criteria for AUD.
- **One in five Canadians** drink more than they drank before the beginning of the COVID 19 pandemic.

ALCOHOL-RELATED HARMS

Alcohol use, and specifically the consumption of alcohol above recommended daily and weekly limits for safer or “low-risk” use, is a serious public health issue.

- In BC, there were ~27 alcohol-related deaths per 100,000 people in 2014, which was more than 3 times higher than the mortality rate for all illicit drugs combined
- From 2002 to 2014, hospitalization rates for alcohol-attributable conditions increased from 383 to 513 per 100,000 individuals
- From 2001 to 2011, the number of primary care visits for alcohol-attributable conditions in BC increased by 53%

https://www.bccsu.ca/wp-content/uploads/2021/01/AUD-Summary-of-Recommendations_01.21.pdf

https://www.canada.ca/en/health-canada/news/2021/01/government-of-canada-supports-first-national-guideline-on-high-risk-drinking-and-alcohol-use-disorder.html

https://www150.statcan.gc.ca/n1/pub/82-624-x/2013001/article/11855-eng.htm

WHO to screen for alcohol use disorder

SECTION A: Screening for AUD

All patients should be screened routinely (e.g. annually or when indicators are observed) with a recommended tool like the AUDIT.[2,3] It is important to screen all patients and not just patients eliciting an index of suspicion for AUD, since most persons with AUD are not recognized.[4]

Consider screening for AUD when any of the following indicators are observed:

- After a recent motor vehicle accident
- Frequent work avoidance (off work slips)
- Rosacea
- Rhinophyma
- High blood pressure
- Cardiac arrhythmia
- Insomnia
- Exacerbation of sleep apnea
- Liver disease
- Chronic pain
- Social problems
- Legal problems

Special Patient Populations

A few studies have reviewed AUD in specific patient populations, including youth, older adults and pregnant or breastfeeding patients. The AUDIT screening tool considered these populations in determining the sensitivity of the tool.

Youth [5]

Older Adults [6,7]

Pregnant or Breastfeeding [2,5]

Screening and Behavioral Counseling Interventions to Reduce Unhealthy Alcohol Use in Adolescents and Adults: Clinical Summary of the USPSTF Recommendation

TABLE 1

Screening and Behavioral Counseling Interventions to Reduce Unhealthy Alcohol Use in Adolescents and Adults: Clinical Summary of the USPSTF Recommendation

Population	Adults, including pregnant women	Adolescents
Recommendations	Screen for unhealthy alcohol use and provide persons engaged in risky or hazardous drinking with brief behavioral counseling interventions. Grade: B	No recommendation. Grade: I (insufficient evidence)

RECOMMENDATION # 4:

All patients (including older adults) should be screened for alcohol use at least annually (i.e., as part of his or her regular physical examination) and at transitions of care (e.g., admission to hospital). Screening should be conducted more frequently if consumption levels exceed the low-risk drinking guidelines, there are symptoms of an AUD, there is a family history of AUD, the patient currently experiences anxiety and/or depression, caregivers express concern, or the older adult is undergoing major life changes or transitions. [**GRADE: Evidence: Moderate; Strength: Strong**]

https://www.aafp.org/pubs/afp/issues/2019/0615/od1.html

https://ccsmh.ca/wp-content/uploads/2019/12/Final_Alcohol_Use_DisorderV6.pdf

https://cep.health/media/uploaded/20191003-CEP_AUD-rev.12_UPDATED.pdf

HOW to screen for alcohol use disorder

The AUDIT Alcohol Consumption Questions (AUDIT-C)

An Effective Brief Screening Test for Problem Drinking

Kristen Bush, MPH; Daniel R. Kivlahan, PhD; Mary B. McDonell, MS; et al

» Author Affiliations | Article Information

Arch Intern Med. 1998;158(16):1789-1795. doi:10.1001/archinte.158.16.1789

We found that the 3 questions of the AUDIT dealing with alcohol consumption (AUDIT-C) performed better than the full AUDIT for identification of heavy drinkers who might benefit from brief primary care interventions.[14] In addition, there was no significant difference between the 2 screening questionnaires for identification of patients with heavy drinking and/or active alcohol abuse or dependence. For identification of active alcohol abuse and/or dependence alone, however, the full AUDIT performed slightly better than the AUDIT-C. However, the AUDIT-C performed better than the commonly recommended CAGE screen (AUROC, 0.717), which identified only 56% of patients in the same population with heavy drinking and/or active alcohol abuse or dependence using the standard cutoff of 2 or more.[20]

https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/208954

How often did you have a drink containing alcohol in the past year?	**Never**	**0**
	Monthly or less	+1
	Two to four times a month	+2
	Two to three times per week	+3
	Four or more times a week	+4
How many drinks containing alcohol did you have on a typical day when you were drinking in the past year?	**1 or 2 drinks**	**0**
	3 or 4	+1
	5 or 6	+2
	7 to 9	+3
	10 or more	+4
How often did you have six or more drinks on one occasion in the past year?	**Never**	**0**
	Less than monthly	+1
	Monthly	+2
	Weekly	+3
	Daily or almost daily	+4

The AUDIT-C is scored on a scale of 0-12 (scores of 0 reflect no alcohol use). In men, a score of 4 or more is considered positive; in women, a score of 3 or more is considered positive. Generally, the higher the AUDIT-C score, the more likely it is that the patient's drinking is affecting his/her health and safety.

Diagnosis of Substance Use Disorder (DSMV)

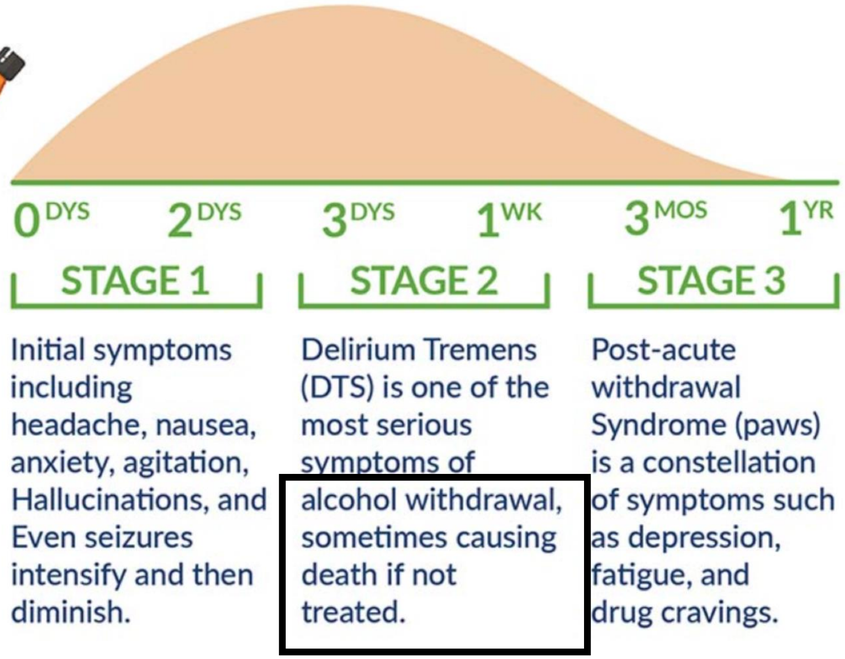
Chronic and Relapsing Condition

1. Taking the substance in larger amounts or for longer than you meant to
2. Wanting to cut down or stop using the substance but not managing to
3. Spending a lot of time getting, using, or recovering from use of the substance
4. Cravings and urges to use the substance
5. Not managing to do what you should at work, home or school, because of substance use
6. Continuing to use, even when it causes problems in relationships
7. Giving up important social, occupational or recreational activities because of substance use
8. Using substances again and again, even when it puts you in danger
9. Continuing to use, even when you know you have a physical or psychological problem that could have been caused or made worse by the substance
10. Needing more of the substance to get the effect you want (tolerance)
11. Development of withdrawal symptoms, which can be relieved by taking more of the substance.

Mild: 2-3 criteria
Moderate: 4-5 criteria
Severe: More than 5 criteria

Alcohol Withdrawal symptoms

ALCOHOL WITHDRAWAL TIMELINE

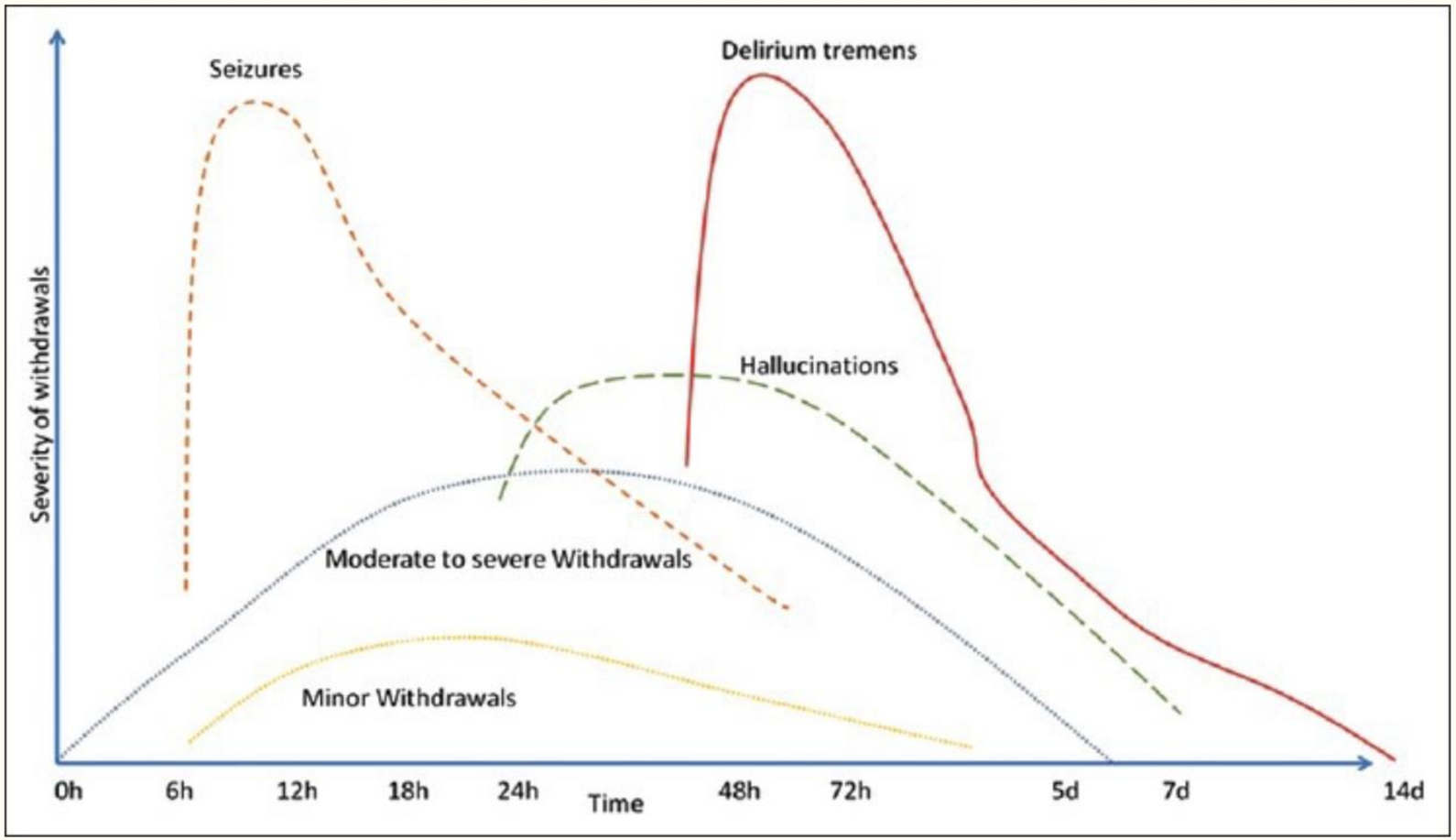


Alcohol on neurotransmitter systems

neurotransmitter	acute intoxication	alcohol withdrawal
Gamma aminobutyric acid (GABA)	↑	↓
N-methyl-d-aspartate (NMDA) excitatory glutamate receptors	↓	↑

https://www.beachhouserehabcenter.com/alcohol-detox-guide/

Stages of alcohol withdrawal



Having one seizure puts the patient at increased risk of developing another seizure at the next time they are in withdrawal.

https://www.researchgate.net/figure/Graph-depicting-the-time-course-of-alcohol-withdrawal-symptoms-based-on-clinical_fig2_263860038

Withdrawal Management

- **Hospital/inpatient treatment:**
  - Risk factors for complicated withdrawal (previous DT's or seizures associated with withdrawal or a poor social support system).

- **Outpatient treatment:**
  - No previous complicated withdrawal
  - No unstable medical or psychiatric conditions
  - Social support

Table 2. Contraindications to Outpatient Treatment of Alcohol Withdrawal Syndrome

Abnormal laboratory results
Absence of a support network
Acute illness
High risk of delirium tremens
History of a withdrawal seizure
Long-term intake of large amounts of alcohol
Poorly controlled chronic medical conditions (e.g., diabetes mellitus, chronic obstructive pulmonary disease, congestive heart failure)
Serious psychiatric conditions (e.g., suicidal ideation, psychosis)
Severe alcohol withdrawal symptoms
Urine drug screen positive for other substances

Adapted from Myrick H, Anton RF. Treatment of alcohol withdrawal. Alcohol Health Res World. *1998;22(1):40.*

https://www.aafp.org/pubs/afp/issues/2013/1101/p589.html

How to assess the need for in patient withdrawal management

The "Prediction of Alcohol Withdrawal Severity Scale" (PAWSS): systematic literature review an pilot study of a new scale for the prediction of complicated alcohol withdrawal syndrome

José R Maldonado [1], Yelizaveta Sher [2], Judith F Ashouri [3], Kelsey Hills-Evans [4], Heavenly Swendsen [5], Sermsak Lolak [6], Anne Catherine Miller [7]

Affiliations + expand

PMID: 24657098 DOI: 10.1016/j.alcohol.2014.01.004

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Prediction of Alcohol Withdrawal Severity Scale (PAWSS)

Maldonado et al., 2014

Part A: Threshold Criteria: (1 point either)

1. Have you consumed any amount of alcohol (i.e., been drinking) within the last 30 days?

   OR did the patient have a "+" BAL upon admission? ____

   IF the answer to either is YES, proceed with test:

Part B: Based on patient interview: (1 point each)

2. Have you ever experienced previous episodes of alcohol withdrawal? ____
3. Have you ever experienced alcohol withdrawal seizures? ____
4. Have you ever experienced delirium tremens or DT's? ____
5. Have you ever undergone of alcohol rehabilitation treatment? ____

   (i.e., in-patient or out-patient treatment programs or AA attendance)
6. Have you ever experienced blackouts? ____
7. Have you combined alcohol with other "downers" like benzodiazepines or barbiturates during the last 90 days? ____
8. Have you combined alcohol with any other substance of abuse during the last 90 days? ____

Part C: Based on clinical evidence: (1 point each)

9. Was the patient's blood alcohol level (BAL) on presentation > 200? ____
10. Is there evidence of increased autonomic activity?

    (e.g., HR > 120 bpm, tremor, sweating, agitation, nausea) ____

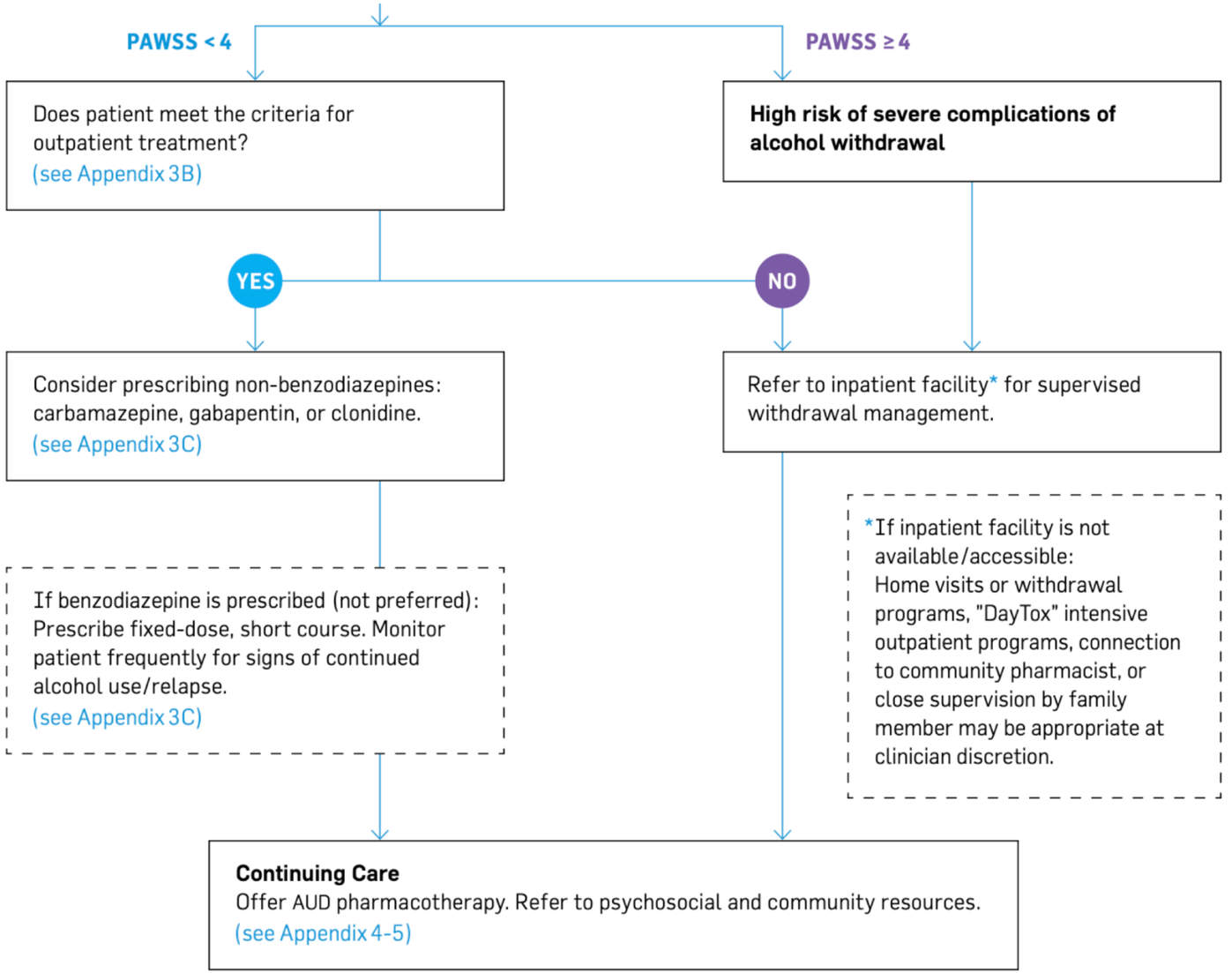
Total Score: ____

Notes: Maximum score = 10. This instrument is intended as a SCREENING TOOL. The greater the number of positive findings, the higher the risk for the development of alcohol withdrawal syndromes. A score of ≥ 4 suggests HIGH RISK for moderate to severe AWS; prophylaxis and/or treatment may be indicated.

Fig. 2. PAWSS tool.

https://www.psychdb.com/_media/addictions/etoh_pawss_score_maldonando_.pdf

How to assess the need for inpatient vs outpatient withdrawal management



Medications used in ACUTE alcohol withdrawal

PHARMACOLOGICAL TREATMENTS FOR WITHDRAWAL			
	Gabapentine[1,2]	Benzodiazepines	
		Diazepam	Lorazepam[1]
Onset of action (PO)	Slow	Rapid (30 min)	Intermediate (30-60 min)
Duration of action	Intermediate	Long	Intermediate
Active metabolites	No	Yes	No
Mild to moderate withdrawal syndrome with a low risk of complications (CIWA-Ar score < 19 or Modified CIWA score < 12 and PAWSS score < 4) OU **Low risk of developing withdrawal syndrome**	100-300 mg PO TID (+/- PRN). Increase gradually to a maximum of 1800 mg daily as tolerated Renal impairment: **CrCl 30 to 59 ml/min:** Limit to 300 mg PO BID **CrCl 15 to 29 ml/min:** Limit to 300 mg PO QD **CrCl < 15 ml/min:** Initiate and limit to 100 mg PO QD Adjust the dose for patients over 65 years of age[3]	5-10 mg PO q 4 to 6 h PRN **OR** 5-10 mg PO TID or QID (+/- HS PRN) Adjust the dose and, when possible, avoid in patients over 65 years of age, especially in an outpatient setting.[3]	1-2 mg PO/SL q 4 to 6 h PRN **OR** 1-2 mg PO/SL TID or QID (+/- HS PRN) Adjust the dose for patients over 65 years of age[3]
Severe withdrawal syndrome[4] (CIWA-Ar score ≥ 19 or Modified CIWA score ≥ 12)	⊗	10-20 mg q 1 to 2 h PRN (preferably via the parenteral route[5])	2-4 mg q 1 to 2 h PRN (preferably via the parenteral route)

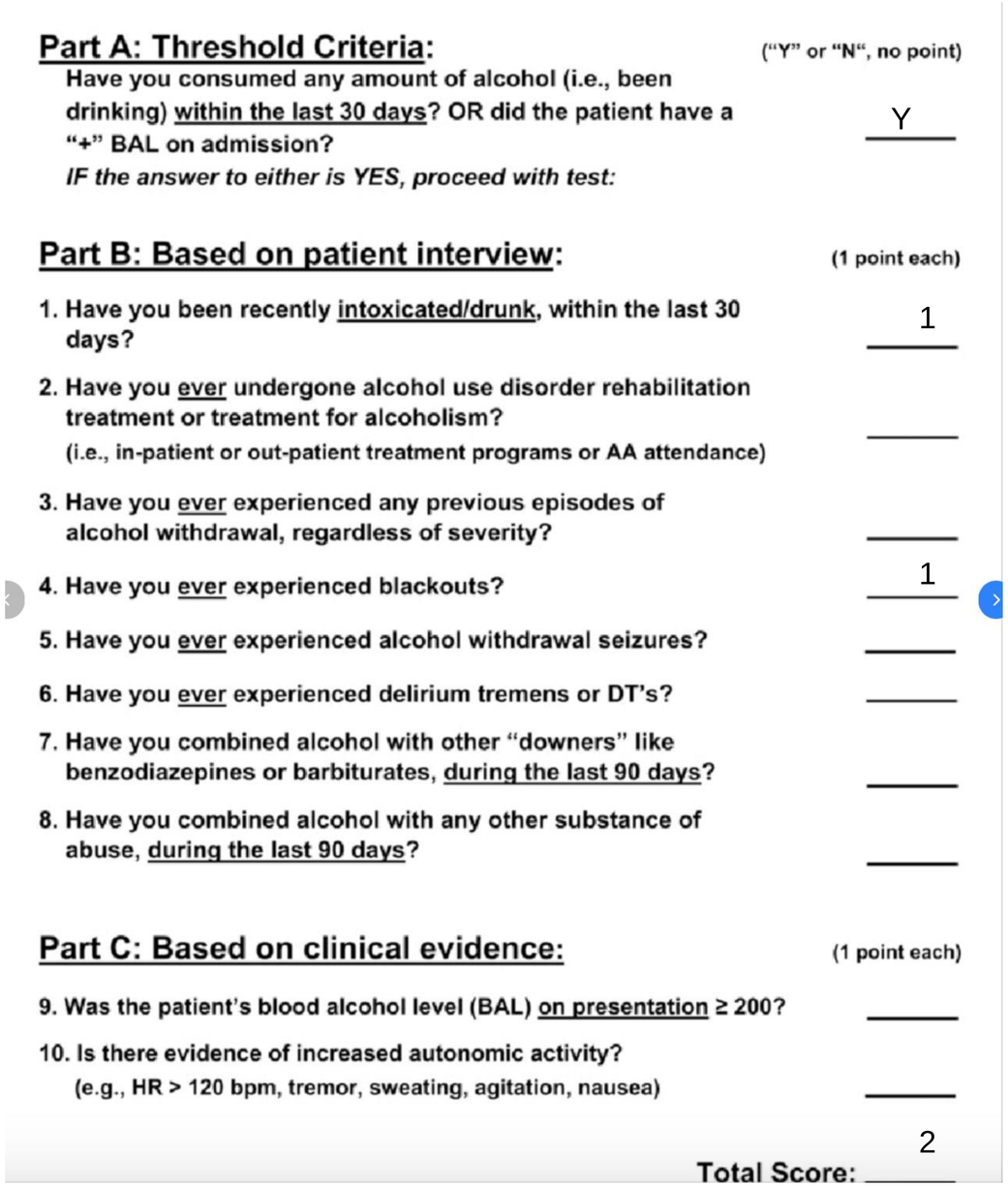
Case OP

- You see a 37 year old female who you have diagnosed with an alcohol use disorder. She has never been ready to stop or cut down on her drinking before, but tells you today she wants to stop drinking as soon as possible. You ask about risk factors for a complicated withdrawal.

- She is not elderly, she has never had seizures or DTs and she has no other co morbidities. She would prefer an outpatient withdrawal since she has work and some responsibilities at home. She comes to the appointment with her partner who seems to be very supportive of her plan to stop drinking.

Case OP continued

- She scores a 2 on her PAWS score, you decide it is safe to do an outpatient withdrawal plan with her. You will ensure close follow up yourself or someone on your team.



Part A: Threshold Criteria: ("Y" or "N", no point)

Have you consumed any amount of alcohol (i.e., been drinking) within the last 30 days? OR did the patient have a "+" BAL on admission? — Y

IF the answer to either is YES, proceed with test:

Part B: Based on patient interview: (1 point each)

1. Have you been recently intoxicated/drunk, within the last 30 days? — 1
2. Have you ever undergone alcohol use disorder rehabilitation treatment or treatment for alcoholism? (i.e., in-patient or out-patient treatment programs or AA attendance) — ____
3. Have you ever experienced any previous episodes of alcohol withdrawal, regardless of severity? — ____
4. Have you ever experienced blackouts? — 1
5. Have you ever experienced alcohol withdrawal seizures? — ____
6. Have you ever experienced delirium tremens or DT's? — ____
7. Have you combined alcohol with other "downers" like benzodiazepines or barbiturates, during the last 90 days? — ____
8. Have you combined alcohol with any other substance of abuse, during the last 90 days? — ____

Part C: Based on clinical evidence: (1 point each)

9. Was the patient's blood alcohol level (BAL) on presentation ≥ 200? — ____
10. Is there evidence of increased autonomic activity? (e.g., HR > 120 bpm, tremor, sweating, agitation, nausea) — ____

Total Score: 2

Case OP continued

- Since you have … en her alcohol use.
- What blood wor…

BASIC BLOOD WORK	AS NEEDED, depending on the following specific clinical situations:	
☐ CBC	☐ β-HCG	Women of child-bearing potential
☐ INR	STBBI SCREENING	
☐ Creatinine	Hepatitis B:	In the presence of risk factors[1]
☐ Electrolytes	☐ HBsAg	
☐ Magnesium	AND	
☐ Albumin	☐ Anti-HBs	
☐ Total bilirubin	Hepatitis C:	
☐ ALT	☐ Anti-HCV, if no positive serology hasbeen documented	
☐ ! ***AST***	OR	
☐ Alkaline phosphatase	☐ HCV RNA screen, if documented positive anti-HCV serology	
☐ Glucose	☐ HIV	
	☐ Syphilis	

https://www.inesss.qc.ca/fileadmin/doc/INESSS/Ordonnances_collectives/Sevrage/INESSS_Blood_work_alcohol_NMP.pdf

Outpatient alcohol withdrawal management (option 1)

☐ Diazepam

***Diazepam to lorazepam conversion 10:1

⚠ **When possible, avoid in patients over 65 years of age.**
⚠ **Not recommended in patients with severe liver impairment, severe or chronic respiratory impairment, sleep apnea, acute closed-angle glaucoma or myasthenia gravis.**
⚠ **If drowsiness, skip this medication.**
⚠ **Inform the physician if more than 60 mg have been given during the past 12 hours.**

Lorazepam

Dosage regimen: ☐ Symptom-triggered (PRN) ☐ Fixed-dose schedule

☐ Diazepam _____ mg PO _(frequency)_ x _____ days, (nb of tablets: ____), then

☐ Diazepam _____ mg PO _(frequency)_ x _____ days, (nb of tablets: ____), then

☐ Diazepam _____ mg PO _(frequency)_ x _____ days, (nb of tablets: ____), then

☐ Diazepam _____ mg PO _(frequency)_ x _____ days, (nb of tablets: ____), then

☐ Diazepam _____ mg PO _(frequency)_ x _____ days, (nb of tablets: ____).

Additional doses (in addition to the regular doses), if necessary:

☐ Diazepam _____ mg PO HS PRN (nb of tablets: ____).

Recommended dosage

Symptom-triggered dosage regimen:
5-10 mg PO q 4 to 6 h PRN.

Decreasing fixed-dose schedule:
5-10 mg PO TID or QID (+/- HS PRN).

⚠ In patients over 65 years of age, start with lower doses to reduce the risk of falls or respiratory depression.

When the patient's condition is stabilized, decrease over 3 to 7 days by reducing the dose or frequency (e.g., TID for 48-72 hours, then BID for 48-72 hours, then HS for 48-72 hours if benzodiazepines are not taken on a regular basis).

https://www.inesss.qc.ca/fileadmin/doc/INESSS/Rapports/Usage_optimal/INESSS_OIPI_outpatient.pdf

Why do we use benzodiazepines?

- It is believed that the provision of BZs alleviates the acute deficiency of GABA neurotransmitter activity that occurs with sudden cessation of alcohol intake.

- Trials comparing different BZs indicate that all are similarly efficacious in reducing signs and symptoms of withdrawal. However long acting agents such as diazepam may be more effective in preventing seizures and delirium tremens.

> Prolonged over-sedation is avoided when diazepam is used for the treatment of alcohol withdrawal, even in elderly patients and patients with liver disease, if dosing is symptom based.
>
> Inter-dose alcohol withdrawal symptoms and rebound phenomena are more likely with lorazepam and oxazepam treatment than with diazepam treatment.
>
> Oral diazepam has a shorter time to peak effect than oral chlordiazepoxide, lorazepam, and oxazepam, which facilitates more rapid treatment and accurate titration to avoid under- or over-treatment when an oral benzodiazepine is used to treat alcohol withdrawal.

https://emcrit.org/wp-content/uploads/2009/09/Diazepam-in-the-Treatment-of-Moderate-to-Severe-Alcohol-Withdrawal.pdf

Outpatient alcohol withdrawal management (option 2)

Treatment of withdrawal syndrome
Choose only one drug

☐ Gabapentin

⚠ **Only for patients with mild to moderate withdrawal syndrome with a low risk of complications and patients at low risk for developing withdrawal syndrome.**	
Regular doses: ☐ Gabapentin _____ mg PO _(frequency)_ on a regular basis x _____ days, then ☐ Gabapentin _____ mg PO _(frequency)_ on a regular basis x _____ days, then ☐ Gabapentin _____ mg PO _(frequency)_ on a regular basis x _____ days, then ☐ Gabapentin _____ mg PO _(frequency)_ on a regular basis x _____ days, then ☐ Gabapentin _____ mg PO _(frequency)_ on a regular basis x _____ days. *Additional doses (in addition to the regular doses), if necessary:* ☐ Gabapentin _____ mg PO _(frequency)_ PRN between doses (nb of tablets: ___) ☐ Gabapentin _____ mg PO HS PRN (nb of tablets: ___).	**Recommended dosage** 100-300 mg PO TID (+/- PRN). Increase gradually to a maximum of **1800 mg per day** as tolerated. Creatinine clearance (CrCl) between 30 and 59 ml/min: limit to 300 mg PO BID. CrCl between 15 and 29 ml/min: limit to 300 mg PO QD. CrCl < 15 ml/min: limit to 100 mg QD. ⚠ In patients over 65 years of age, start with lower doses to reduce the risk of falls or respiratory depression. When the patient's condition is stabilized, decrease stepwise by 100 to 200 mg PO TID over 3 to 7 days, unless gabapentin is continued for relapse prevention, in which case refer to INESSS's Québec national medical protocol No. 888027.

Using gabapentin instead of BZs

Gabapentin for alcohol use disorder: A good option, or cause for concern?

Vania Modesto-Lowe, MD, MPH, Gregory C. Barron, MD, Benjamin Aronow, BS and Margaret Chaplin, MD

Cleveland Clinic Journal of Medicine December 2019, 86 (12) 815-823; DOI: https://doi.org/10.3949/ccjm.86a.18128

KEY POINTS

- Gabapentin has been shown to be safe and effective for mild alcohol withdrawal but is not appropriate as mono-therapy for severe withdrawal owing to risk of seizures.
- During early abstinence, gabapentin may improve sleep, cravings, and mood—factors associated with relapse.
- Gabapentin is being used recreationally to achieve or enhance euphoria, but its misuse potential appears to be low when taken at therapeutic doses by patients without a history of drug abuse.

Gabapentin is believed to decrease excitation of the central nervous system in multiple ways:

- It reduces the release of glutamate, a key component of the excitatory system[16]
- It increases the concentration of gamma-aminobutyric acid (GABA), the main inhibitory neurotransmitter in the brain[7]
- By binding the alpha-2-delta type 1 subunit of voltage-sensitive calcium channels,[8,15–17] it inhibits excitatory synapse formation independent of calcium channel activity[16]
- By blocking excitatory neurotransmission, it also may indirectly increase the concentration of GABA in the central nervous system[16,17]
- It modulates action of glutamic acid decarboxylase (involved in the synthesis of GABA) and glutamate synthesizing enzyme to increase GABA and decrease glutamate.[17]

https://www.ccjm.org/content/86/12/815

Example of a prescription model (option 1)

***Diazepam to lorazepam conversion 10:1

TIPS:
- I would personally have this dispensed daily for safety reasons (this way the pharmacist can also see the patient daily).
- Patient should be encouraged to not mix alcohol with the BZs.
- Should not be used if suspicion for BZUD.
- If not working and continues to have severe withdrawal symptoms, go to ER.

☐ Diazepam

⚠ **When possible, avoid in patients over 65 years of age.**
⚠ **Not recommended in patients with severe liver impairment, severe or chronic respiratory impairment, sleep apnea, acute closed-angle glaucoma or myasthenia gravis.**
⚠ **If drowsiness, skip this medication.**
⚠ **Inform the physician if more than 60 mg have been given during the past 12 hours.**

Dosage regimen: ☐ Symptom-triggered (PRN) ☐ Fixed-dose schedule

☐ Diazepam 10 mg PO QID x 2 days, (nb of tablets: ____), then
☐ Diazepam 10 mg PO TID x 2 days, (nb of tablets: ____), then
☐ Diazepam 10 mg PO BID x 2 days, (nb of tablets: ____), then
☐ Diazepam 10 mg PO QD x 2 days, (nb of tablets: ____), then
☐ Diazepam _____ mg PO (frequency) x _____ days, (nb of tablets: ____).

Additional doses (in addition to the regular doses), if necessary:

☐ Diazepam _____ mg PO HS PRN (nb of tablets: ____).

Recommended dosage

Symptom-triggered dosage regimen:
5-10 mg PO q 4 to 6 h PRN.

Decreasing fixed-dose schedule:
5-10 mg PO TID or QID (+/- HS PRN).

⚠ In patients over 65 years of age, start with lower doses to reduce the risk of falls or respiratory depression.

When the patient's condition is stabilized, decrease over 3 to 7 days by reducing the dose or frequency (e.g., TID for 48-72 hours, then BID for 48-72 hours, then HS for 48-72 hours if benzodiazepines are not taken on a regular basis).

Example of a prescription model (option 2)

Treatment of withdrawal syndrome
Choose only one drug

☐ Gabapentin

⚠ **Only for patients with mild to moderate withdrawal syndrome with a low risk of complications and patients at low risk for developing withdrawal syndrome.**

Regular doses:

☐ Gabapentin 100 mg PO TID (frequency) on a regular basis x 2 days, then

☐ Gabapentin 200 mg PO TID (frequency) on a regular basis x 2 days, then

☐ Gabapentin 300 mg PO TID (frequency) on a regular basis x 2 days, then

☐ Gabapentin _____ mg PO _____ (frequency) on a regular basis x _____ days, then

☐ Gabapentin _____ mg PO _____ (frequency) on a regular basis x _____ days.

Additional doses (in addition to the regular doses), if necessary:

☐ Gabapentin _____ mg PO _____ (frequency) PRN between doses (nb of tablets: ___)

☐ Gabapentin _____ mg PO HS PRN (nb of tablets: ___).

Recommended dosage

100-300 mg PO TID (+/- PRN). Increase gradually to a maximum of **1800 mg per day** as tolerated.

Creatinine clearance (CrCl) between 30 and 59 ml/min: limit to 300 mg PO BID.

CrCl between 15 and 29 ml/min: limit to 300 mg PO QD.

CrCl < 15 ml/min: limit to 100 mg QD.

⚠ In patients over 65 years of age, start with lower doses to reduce the risk of falls or respiratory depression.

When the patient's condition is stabilized, decrease stepwise by 100 to 200 mg PO TID over 3 to 7 days, unless gabapentin is continued for relapse prevention, in which case refer to INESSS's Québec national medical protocol No. 888027.

https://www.inesss.qc.ca/fileadmin/doc/INESSS/Rapports/Usage_optimal/INESSS_OIPI_outpatient.pdf

Case OP continued

- You and her decide to go ahead with diazepam prescription.
- Your nurse calls her on day 3.

- Ms. CM tells you she has some mild withdrawal symptoms, but she feels well and wants to continue. She has not drank any alcohol since she started either. (HERE- you may need to adjust her dose if she is too drowsy or she is having too many withdrawal symptoms). Example: You may need to extend the diazepam 10mg po BID for another 2 days if taper is too fast.

- You also ensure that she is taking the vitamins as prescribed.
  - Thiamine 100mg po BID
  - Multivitamin
  - Folic acid 5mg po die
  - Vitamin B 6 (pyridoxine) 50mg po die
  - Consider pantoprazole for the first couple of days to weeks
  - May need to replace magnesium (takes about 72 hours to see a difference in level)

Case OP continued

- You speak to the patient on day 7 and she is feeling quite well but admits that she has alot of cravings but has not drank any alcohol yet. Other than meetings and psychological help, she was wondering if you could give her any medications to help with this.

Québec resources

- Detox centres: Medical observation for detox of the drug (ex: alcohol and BZs). CHUM has some beds dedicated to this. Always inpatient.
- Rehab centers- can be inpatient or outpatient. Not medically supervised. CRD in Quebec per region.
- Outpatient clinics- Herzl Addiction Center, some CLSCs and CHUM.
- Outpatient resources- Some CLSCs have peer support workers. There are AA groups as well (virtual and in person now available).

Relapse Prevention Medication

This is NOT management of acute withdrawal

PHARMACOTHERAPY FOR RELAPSE PREVENTION		
Drug	**Starting dose**	**Details for making adjustment up to the target treatment dose**
First-line therapy		**Can be used at 100mg - 150mg po die OFF LABEL**
Naltrexone	25 mg PO QD	Increase dose to 50 mg after 2 to 4 days, as tolerated
If naltrexone cannot be administered[1] (Allergy, intolerance, opioid use in the past 10 days, or opioid use anticipated (e.g., elective surgery with opioid prescription) or opioid use disorder, liver failure, cirrhosis, ↑ liver function test results to more than 2.5 times ULN or acute hepatitis)		
Acamprosate *Reserved for use by an authorized prescriber[2]*	Clcr ≥ 50 ml/min and ≥ 60 kg:	666 mg PO TID
	Clcr ≥ 50 ml/min and < 60 kg:	666 mg PO AM, 333 mg PO PM and 333 mg PO HS
	Clcr 30 to 49 ml/min:	333 mg PO TID

	Naltrexone	**Acamprosate** ***Exceptional medication[1]***
Most frequent or serious adverse effects	- Nausea, vomiting, abdominal cramps - Anxiety, insomnia - Headaches - Risk of suicidal thoughts	- Diarrhea (dose-dependent) - Drowsiness, dizziness, insomnia, unusual fatigue - Risk of suicidal thoughts
Most significant drug interactions	- Concomitant use of other potentially hepatotoxic medications - Opioids: naltrexone may ↓ the effect and precipitate opioid withdrawal syndrome	- None

https://www.inesss.qc.ca/fileadmin/doc/INESSS/Ordonnances_collectives/Sevrage/INESSS_Relapse_alcohol_NMP.pdf

Naltrexone- reducing the reward associated with drinking

The status of naltrexone in the treatment of alcohol dependence: specific effects on heavy drinking

Helen M Pettinati [1], Charles P O'Brien, Amanda R Rabinowitz, Shoshana P Wortman, David W Oslin, Kyle M Kampman, Charles A Dackis

Affiliations + expand

PMID: 17110818 DOI: 10.1097/01.jcp.0000245566.52401.20

Naltrexone in the treatment of alcohol dependence: a Canadian trial

Myroslava K Romach [1], Edward M Sellers, Gail R Somer, Michel Landry, Graeme M Cunningham, Roman D Jovey, Charles McKay, Jean Boislard, Céline Mercier, Jean-Marc Pépin, Jean Perreault, Eliane Lemire, Raymond P Baker, William Campbell, Daniel Ryan

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PMID: 12422250

Maintenance of alcohol use disorder treatment

LABORATORY TESTS BY TREATMENT	
	ALT, AST, albumin, total bilirubin, INR
Naltrexone	4 to 6 weeks after the start of treatment, then every 6 months
Acamprosate	NR
Gabapentin	NR
Topiramate	NR

Acronyms and abbreviations: ALT: alanine aminotransferase; AST: aspartate aminotransferase; INR: international normalized ratio; NR: not recommended

No real end date for these medications. Can be taken for 12 weeks up to ?lifetime

FOLLOW-UP

- Patients should be monitored closely at the start of treatment (e.g., once a week). This should include checking or checking for the following:
  - The onset or worsening of sleep disturbances, symptoms of depression or anxiety, or suicidal ideation, even without alcohol use;
  - The onset of withdrawal symptoms, especially for patients without prior withdrawal management;
  - Tolerance of and compliance with the treatment, and cravings for alcohol.
- Next, a follow-up should be conducted at least once a month for 6 months by a member of the multidisciplinary team (except the psychosocial workers) and with reduced but regular frequency if the treatment is continued beyond 6 months.
- It may be beneficial to take steps to promote therapeutic compliance:
  - In the event of therapeutic noncompliance (rather than discontinuing the medication);
  - In the event of instability or social precariousness (e.g., homelessness).
- Additional follow-ups, depending on the medication:
  - Topiramate: Monitor the patient for the onset of metabolic acidosis;
  - Naltrexone: A liver profile should be run 4 to 6 weeks after the start of treatment and every 6 months thereafter.
- Consideration could be given to referring the patient to a specialized facility or to intensifying the outpatient follow-up, as the case may be, in the following situations:
  - The onset or worsening of a severe, unstable or complex physical or mental health problem (e.g., bipolar disorder or psychotic disorder, such as schizophrenia);
  - The onset or worsening of another substance use disorder, with the exception of tobacco and cannabis;
  - A deterioration in the social environment or psychosocial destabilization;
  - No benefit obtained despite several adequate treatment attempts.
- Following treatment, the absence of AUD criteria for a period of more than 3 months but less than 12 months is considered early remission, whereas a symptom-free period of more than 12 months is considered sustained remission

https://www.inesss.qc.ca/fileadmin/doc/INESSS/Rapports/Usage_optimal/INESSS_GUO_Sevrage_rechute_EN_VF.pdf

https://www.inesss.qc.ca/fileadmin/doc/INESSS/Ordonnances_collectives/Sevrage/INESSS_Relapse_alcohol_NMP.pdf

Case OP continued

- After hearing about all of the options, she decided to go with naltrexone since she likes the once daily dosing. She did LFTs when you saw her one week ago and they are normal.
- You give her blood work requisition to be done in 6 weeks to ensure no change in her liver status. (Monograph suggests to discontinue naltrexone if LFTs increase by >/= 3 times). Please evaluate risk and benefits with the patient.
- She is connected with an AA group in the community as well as her local CRD.

Case OP continued

- You call the patient back in one month to see how she is doing with the naltrexone.
- She finds the medication is working well for her alcohol use disorder and her cravings but finds she sleeps alot and is quite depressed since she has stopped drinking.
- You speak to her and diagnose with her MDE (mild) and decide to start an SSRI. Which one do you choose?

Co- occurring mental health issues

Psychiatric comorbidities in alcohol use disorder

Alvaro Castillo-Carniglia, Katherine M Keyes, Deborah S Hasin, and Magdalena Cerdá

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MDD	Median (across 35 studies) lifetime alcohol use disorder† in people with MDD: 30%, range 10–60%;[19] ECA survey 16·5% MDD (lifetime)	MDD† in people with lifetime alcohol use disorder 37%;[20] MDD† in people with 12-months alcohol use disorder 4–22%[20]
Attention-deficit hyperactivity disorder	Alcohol use disorder‖ in French students with ADHD 25·9%;[23] alcohol use disorder** in young men enlisting to the Military Service in Australia with ADHD 19·3%[24]	ADHD in adolescents with alcohol use disorder††: 19·9–23·6%;[25] ADHD in adults with alcohol use disorder: 33% (current)[25,26]
Anxiety disorder	Alcohol use disorder in people with any anxiety disorder 20–40%;[20] ECA survey: 17·9% in people with any anxiety disorder, 28·7% in people with panic disorder	ECA survey: 19·4% any lifetime anxiety disorder; NCS survey: 8'6% lifetime GAD in men, 15·7% in women; NCS survey: 3·6% lifetime panic disorder in men, 12·9% in women; NCS survey: 19·3% lifetime social phobia in men, 30·3% in women
PTSD	Alcohol use disorder in young adults with PTSD in the general population of Brazil 34·4%;[30] NESARC-III: 54·5% lifetime alcohol use disorder in people with lifetime PTSD[31]	NCS survey: 10·3% lifetime PTSD in men, 26 ·2% in women; current PTSD in German patients with substance use disorder with alcohol dependence 22·9%[32]

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7006178/

Depression and AUD

A double-blind, placebo-controlled trial combining sertraline and naltrexone for treating co-occurring depression and alcohol dependence

Helen M Pettinati [1], David W Oslin, Kyle M Kampman, William D Dundon, Hu Xie, Thea L Gallis, Charles A Dackis, Charles P O'Brien

Affiliations + expand

PMID: 20231324 PMCID: PMC3121313 DOI: 10.1176/appi.ajp.2009.08060852

Free PMC article

Conclusions: More depressed alcohol-dependent patients receiving the sertraline plus naltrexone combination achieved abstinence from alcohol, had delayed relapse to heavy drinking, reported fewer serious adverse events, and tended to not be depressed by the end of treatment.

https://pubmed.ncbi.nlm.nih.gov/20231324/

End of case OP

- She agrees to be started on sertraline and continue her naltrexone.
- She is also connected with Psychology through CLSC for her co occurring depression and AUD (in short term remission).

Case DA

- You meet with 58 year old male who is well known to you, you have been following him for years. He tells you he is here because his wife thinks he drinks too much. He admits to drinking about 2 glasses of red wine per night and perhaps 3-4 on the weekends for many years now.
- He is not interested in stopping to drink but agrees that he can try to cut down.
- He takes chronic opioids for his back pain, he takes dilaudid 1mg po qhs prn (about 3 times per week).

Case DA continued

- Which of the RPM is contraindicated in this case?
- Naltrexone. Patient must have no opioids in his system for 7-10 days before starting naltrexone.
- Since he does not want to be abstinent, but rather agrees to cut down on his alcohol use, his best option is gabapentin.
- You counsel him on the SEs of gabapentin and recently have blood work that shows his CrCl is normal.

Relapse Prevention Medication

<table>
<tr>
<td>Gabapentin</td>
<td>Clcr ≥ 15 ml/min:
300 mg PO QD HS[3]

Clcr < 15 ml/min:
100 mg PO QD HS[3,4]</td>
<td>
Clcr ≥ 60 ml/min: Uptitrate every 3 days according to the following steps (if well tolerated):
<table>
<tr><th>AM</th><th>PM</th><th>HS</th></tr>
<tr><td>200 mg</td><td>200 mg</td><td>200 mg</td></tr>
<tr><td>300 mg</td><td>300 mg</td><td>300 mg</td></tr>
<tr><td>300 mg</td><td>300 mg</td><td>600 mg</td></tr>
<tr><td>600 mg</td><td>300 mg</td><td>600 mg</td></tr>
<tr><td>600 mg</td><td>600 mg</td><td>600 mg</td></tr>
</table>
Target therapeutic window, depending on tolerance and therapeutic response
Clcr 30 to 59 ml/min: Increase to a dose of 300 mg PO BID after 7 days (if well tolerated)
Clcr 15 to 29 ml/min: Continue with 300 mg PO QD HS
Clcr < 15 ml/min: Continue with 100 mg PO QD HS[4]
</td>
</tr>
<tr>
<td>Topiramate
Reserved for use by an authorized prescriber with experience using this drug</td>
<td>25 mg PO QD HS[4]</td>
<td>
Uptitrate every 7 days according to the following steps (if well tolerated):
Clcr ≥ 70 ml/min:
<table>
<tr><th>AM</th><th>HS</th></tr>
<tr><td>25 mg</td><td>25 mg</td></tr>
<tr><td>25 mg</td><td>50 mg</td></tr>
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</table>
Target therapeutic window, depending on tolerance and therapeutic response
Clcr < 70 ml/min[4]:
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<tr><th>AM</th><th>HS</th></tr>
<tr><td>25 mg</td><td>25 mg</td></tr>
<tr><td>25 mg</td><td>50 mg</td></tr>
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<tr><td>50 mg</td><td>75 mg</td></tr>
<tr><td>75 mg</td><td>75 mg</td></tr>
</table>
Target therapeutic window, depending on tolerance and therapeutic response
</td>
</tr>
</table>

Gabapentin[2]	Topiramate[2]
- Drowsiness, dizziness, fatigue - Tremors, ataxia - Nystagmus - Peripheral edema - Diarrhea - Risk of suicidal thoughts	- Paresthesia - Drowsiness, dizziness, nervousness, cognitive problems, fatigue - Weight loss, decreased appetite - Risk of acute myopia, secondary narrow-angle glaucoma and visual field defects - Renal calculi - Risk of metabolic acidosis - Risk of suicidal thoughts
- Opioids or CNS depressants (including alcohol): ↑ the risk of sedation and respiratory depression - Aluminum- or magnesium-based antacids: ↓ absorption. Take 2 hours before or after gabapentin	- ↓ concentrations and efficacy of oral contraceptives - Others[4]

https://www.inesss.qc.ca/fileadmin/doc/INESSS/Ordonnances_collectives/Sevrage/INESSS_Relapse_alcohol_NMP.pdf

Case DA continued

- You start him on gabapentin 200mg po TID to be taken daily and ensure that **he does not stop drinking cold turkey!** He should continue to drink and can cut down slowly as his cravings are reduced.

- The dose is increased in 3 days to 300mg po TID. He then has a telemedicine follow up with you. He reports no SEs but is not sure that the medication is helping. You decide to increase it again, to 300- 300- 600mg po.

- You speak to him again in 1 month. He now tells you he thinks it might be helping and he has managed to drink a bit less each day. He is not experiencing any withdrawal symptoms.

Gabapentin as relapse prevention medication

Gabapentin Treatment for Alcohol Dependence: A Randomized Controlled Trial

Barbara J. Mason, PhD,[a] Susan Quello, BA, BS,[a] Vivian Goodell, MPH,[a] Farhad Shadan, MD,[b] Mark Kyle, MD,[b] and Adnan Begovic, MD[b]

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Conclusions and Relevance

Gabapentin (particularly the 1800 mg dosage) was effective in treating alcohol dependence and relapse-related symptoms of insomnia, dysphoria and craving, with a favorable safety profile. Increased implementation of pharmacological treatment of alcohol dependence in primary care may be a major benefit of gabapentin as a treatment option for alcohol dependence.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3920987/

End of case DA

- You ensure to speak to him about seeking psychological help as well. Suggest vitamins especially if not eating well.
- You ensure to do blood work given his age and alcohol use. You will include NFLP and HTN screen as well.
- You speak to him again in 6 months and he tells you he is doing well and now only drinks on Friday, Saturday and Sundays.

Summary of how to manage outpatient withdrawal

	AUD and PAWS<4 (wants to be abstinent)	**AUD and PAWS>/= 4 (wants to be abstinent)**	**+/- AUD and PAWS<4 (does not want to be abstinent)**
How?	Rx for outpatient gabapentin vs BZs.	Needs to be referred for in patient detox.	Suggest RPM.
Where?	Home with close follow up. Suggest CRD.	EX: CHUM (514-890-8321) and suggest CRD.	Suggest CRD.
What?	BZs- has had previous withdrawal GB- especially if suspect BZ UD	Will be prescribed BZs based on CIWA score.	Naltrexone Gabapentin

Case OP **Case DA**

Take home points for AUD

- Offer outpatient withdrawal management when safe.
- Ensure they are taking the appropriate vitamins at least until they are back to eating more regularly.
- Encourage relapse prevention medication.
- Encourage Psychological treatment with a Psychologist or AA or the various CRDs in Quebec.

Thank you

Questions?

Can contact me at:
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