CURRENT APPROACHES IN THE TREATMENT OF ALCOHOL USE DISORDER

(WITH A REVIEW OF CANADA'S GUIDANCE ON ALCOHOL AND HEALTH: FINAL REPORT)

Dr. Valerie Primeau, MD FRCPC
Dr. Andriy V Samokhvalov, MD, PhD, FRCPC

Email vmdprimeau@gmail.com for access to materials

Full References Available Upon Request
Canadian Psychiatric Association 2023

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NO CONFLICT OF INTEREST TO DECLARE

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OBJECTIVES

	At the end of this session participants will be able to:
Describe	Describe the evidence-based medications used to treat alcohol use disorder (AUD), from acute withdrawal to community maintenance treatment;
Discuss	Discuss the new 2023 Canada's Guidance on Alcohol and Health: Final Report; and
Identify	Identify the importance of concurrent integrated treatment and recognize the impact of the COVID-19 pandemic on the prevalence and treatment of AUD.

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GUIDELINES & RESOURCES

Canadian Alcohol Use Disorder Guideline Committee

- https://www.cmaj.ca/content/cmaj/195/40/E1364.full.pdf
- Canadian guideline for the clinical management of high-risk drinking and alcohol use disorder (**October 16, 2023**)
- 15 recommendations, recommendation 13 is controversial (to not prescribe antidepressants for concurrent anxiety or mood symptoms)

Ontario Health Quality (previously HQO)

- https://www.hqontario.ca/Portals/0/documents/evidence/quality-standards/qs-alcohol-use-disorder-quality-standard-en.pdf
- Problematic Alcohol Use and Alcohol Use Disorder Quality Standards (2020)

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GUIDELINES & RESOURCES

Canadian Coalition for Seniors Mental Health (CCSMH)

- https://ccsmh.ca/wp-content/uploads/2019/12/Final_Alcohol_Use_DisorderV6.pdf
- Canadian Academy of Geriatric Psychiatry (CAGP)
- Canadian Guidelines on Alcohol Use Disorder Among Older Adults (2019)

American Psychiatric Association (APA)

- https://psychiatryonline.org/doi/pdf/10.1176/appi.books.9781615371969
- The APA Practice Guideline for the Pharmacological Treatment of Patients With Alcohol Use Disorder (2018)

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GUIDELINES & RESOURCES

British Columbia Centre on Substance Use (BCCSU)

- https://www.bccsu.ca/
- Great section on Substance Use and COVID-19
- Provincial guidelines for AUD

Addiction Care and Treatment Online Course (BCCSU and UBC collaboration)

- https://ubccpd.ca/course/addiction-care-and-treatment
- Now up to 20.0 Mainpro+/MOC Section 3 credits per their website

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WHAT IS THE LIFETIME PREVALENCE OF AUD IN CANADA?

(5%, 10%, 20%, 30%?)

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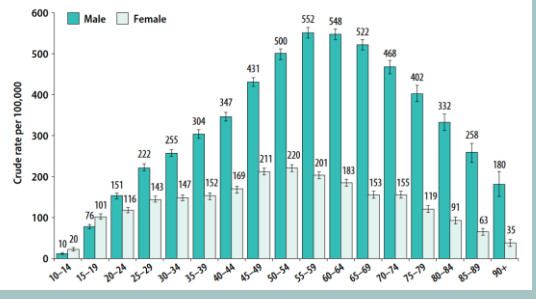
Alcohol is by far the most common drug used by Canadians

- In Canada, there were around 77,000 hospitalizations entirely caused by alcohol in 2015–2016, compared to 75,000 hospitalizations for heart attacks in the same year
- In 2002, alcohol was responsible for 4,258 deaths in Canada, representing 1.9% of all deaths
- Alcohol use disorder (AUD) is the most prevalent Substance Use Disorder with a lifetime prevalence of 18.1% in Canada
- As compared to before the COVID-19 pandemic, 23.3% of respondents reported drinking more alcohol compared to before the pandemic

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



Canadian Centre on Substance Use and Addiction Alcohol Canadian Drug Summary, Fall 2017
CIHR & CCSA 2020-2022

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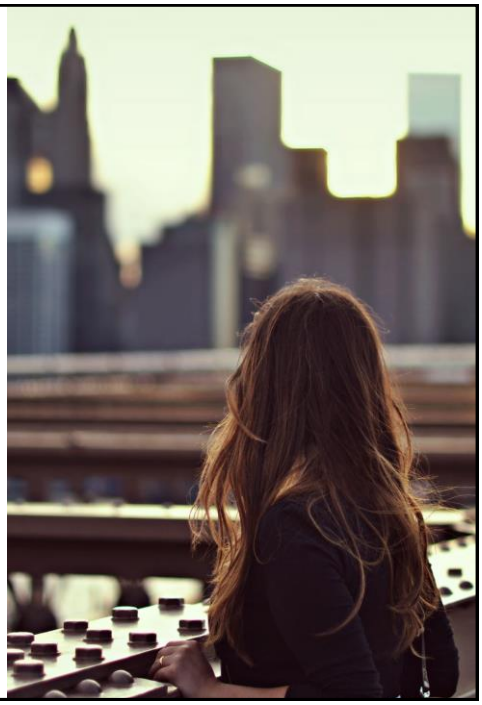
PREVALENCE IN YOUTH

By the time Canadian students are in the 12th grade, the majority of them are drinking alcohol

83% of 12th-grade students in Ontario admitted to drinking alcohol

49% confessing they binge drink



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CO-MORBIDITY WITH MENTAL ILLNESS

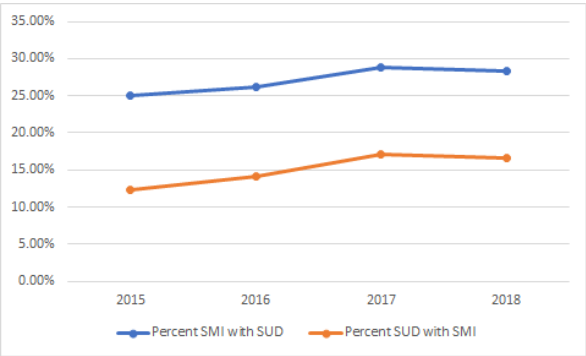
Substance Use Disorders are highly comorbid with virtually all categories of psychiatric disorders, especially psychotic, mood, anxiety, ADHD and personality disorders

Lifetime prevalence of addictive disorder 29% (OR 2.7), 15% for drug disorder

Odds are 7 times greater of developing both alcohol and drug disorders

53% of people with drug disorder have a mental disorder (OR 4.5)

ECA study, 1988



Source: SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, Mental Health, Detailed Tables available at: https://www.samhsa.gov/data/population-data-nsduh

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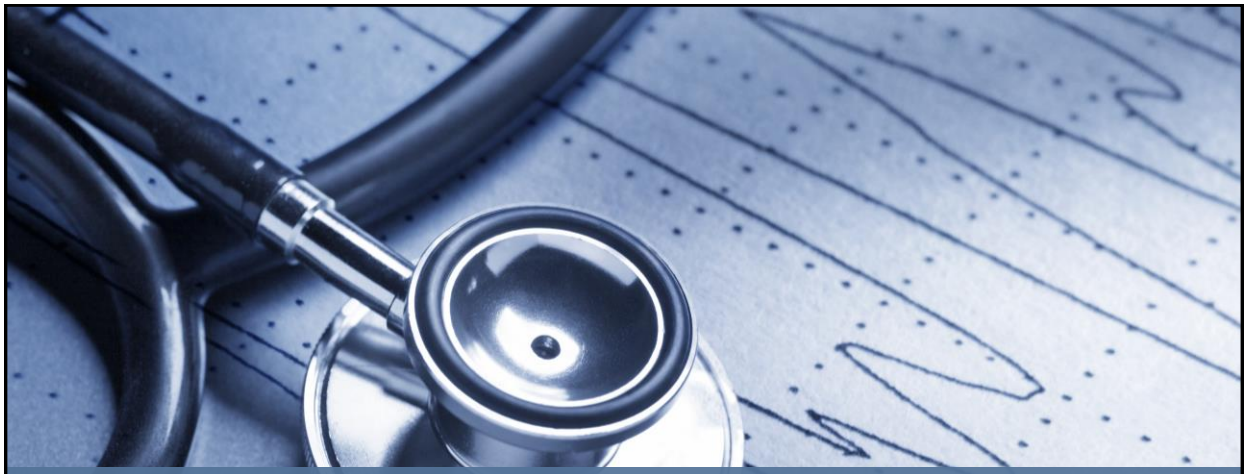

SCREENING

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SCREENING

Most common screening errors in our practice:

Not asking about alcohol use

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)

Not using a clinical scale to measure the impact of the drinking or to measure the cravings

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HOW MANY STANDARD DRINKS DOES THE NEW CANADA'S GUIDANCE ON ALCOHOL AND HEALTH RECOMMEND TO AVOID ALCOHOL-RELATED CONSEQUENCES FOR YOURSELF OR OTHERS?

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Canadian Centre on Substance Use and Addiction

Evidence. Engagement. Impact.

www.ccsa.ca • www.ccdus.ca

Canada's Guidance on Alcohol and Health: Final Report

January 2023

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CANADA'S GUIDANCE ON ALCOHOL AND HEALTH (2023)

Key points from the guidance include:

- There is a continuum of risk associated with weekly alcohol use where the risk of harm is:
  - **0 drinks per week** — Not drinking has benefits, such as better health, and better sleep.
  - **2 standard drinks or less per week —** You are likely to avoid alcohol-related consequences for yourself or others at this level.
  - **3–6 standard drinks per week —** Your risk of developing several types of cancer, including breast and colon cancer, increases at this level.
  - **7 standard drinks or more per week** — Your risk of heart disease or stroke increases significantly at this level.
  - **Each additional standard drink** radically increases the risk of alcohol-related consequences.
- Consuming more than 2 standard drinks per occasion is associated with an increased risk of harms to self and others, including injuries and violence.
- When pregnant or trying to get pregnant, there is no known safe amount of alcohol use.
- When breastfeeding, not drinking alcohol is safest.
- No matter where you are on the continuum, for your health, less alcohol is better.

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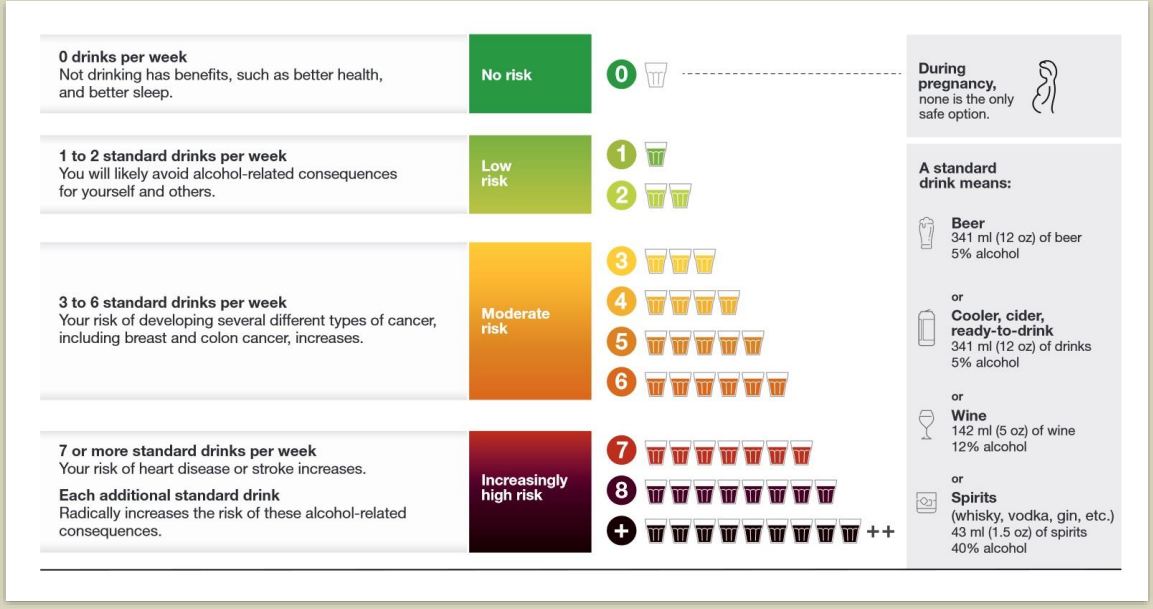

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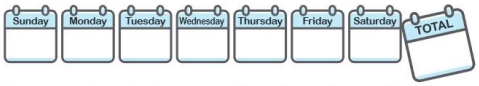
Aim to drink less

Drinking less benefits you and others. It reduces your risk of injury and violence, and many health problems that can shorten life.

Here is a good way to do it

Count how many drinks you have in a week.



Set a weekly drinking target. If you're going to drink, **make sure you don't exceed 2 drinks on any day.**

Good to know

You can reduce your drinking in steps! Every drink counts: any reduction in alcohol use has benefits.

It's time to pick a new target

What will your weekly drinking target be?

0 1 2 3 4 5 6

Tips to help you stay on target

- Stick to the limits you've set for yourself.
- Drink slowly.
- Drink lots of water.
- For every drink of alcohol, have one non-alcoholic drink.
- Choose alcohol-free or low-alcohol beverages.
- Eat before and while you're drinking.
- Have alcohol-free weeks or do alcohol-free activities.

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Table 1: Sample interview questions for DSM-5-TR criteria for diagnosis of alcohol use disorder

Diagnostic criterion*	Question: "In the past year..."
1	Did you drink more or for a longer time than you had originally planned to?
2	Did you try to cut back or stop drinking, but weren't able to?
3	Did you spend a lot of your time drinking or recovering from drinking?
4	Were you so preoccupied with wanting a drink that you found it hard to think about anything else?
5	Did you have a hard time doing your job properly or going to school because of alcohol? Taking care of your family and home?
6	Did you keep drinking even though you knew it was causing problems in your relationships?
7	Did you give up on activities or hobbies, or seeing friends because of drinking?
8	Did you get into dangerous situations more than once because of your drinking? Such as drinking and driving, unsafe sex, other situations where you could have been hurt?
9	Did you keep drinking even though it was making you feel depressed or anxious, or making a physical health problem worse?
10	Did you feel tense and anxious because it takes more drinks than it did in the past to feel intoxicated? Do you find that drinking the same amount as in the past doesn't relieve your stress or have the same effects?
11	Did you ever have shaky hands, sweats, anxiety, hearing voices, nausea or a seizure, hours after you'd stopped drinking? Do you ever have a drink to prevent those symptoms from happening?

Note: DSM-5-TR = *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision*.[11]
*Refers to the numbered DSM-5-TR diagnostic criteria for alcohol use disorder.[11]

CAGE Questionnaire

Have you ever felt you needed to **C**ut down on your drinking?

Have people **A**nnoyed you by criticizing your drinking?

Have you ever felt **G**uilty about drinking?

Have you ever felt you needed a drink first thing in the morning (**E**ye-opener) to steady your nerves or to get rid of a hangover?

Two "yes" responses indicate that the possibility of alcoholism should be investigated further

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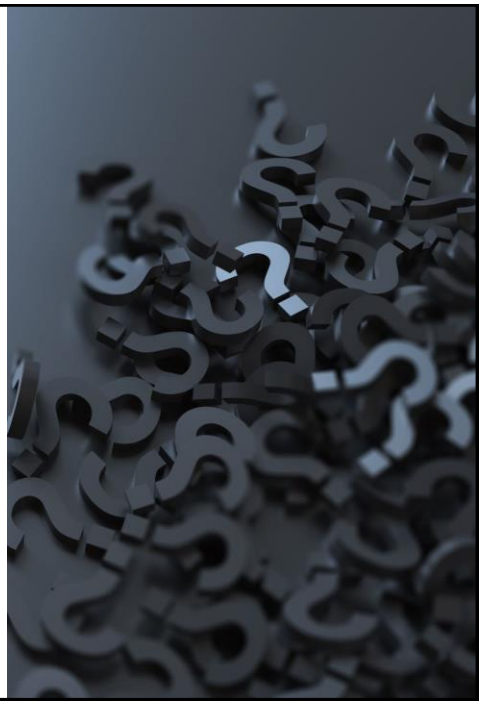
SCREENING

Alcohol Use Disorders Identification Test (AUDIT) developed by WHO

- 3 subsections comprising: hazardous alcohol use (3 questions), symptoms of dependence (3 questions), and harmful alcohol use (4 questions)
- Each question is scored on a 4-point scale, for a total of 40 points, with higher ratings related to higher risk for alcohol related problems
- Scores ranging between 8 and 15 (medium risk for alcohol related problems) are usually targeted by a brief intervention
- Scores of 16 to 19 may be indicative of hazardous use of alcohol, while scores above 20 are concerning for alcohol dependence



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CRAVING SCALES

Assessing Alcohol Problems: A Guide for Clinicians and Researchers

Penn Alcohol Craving Scale (PACS)

PLEASE READ EACH ITEM CAREFULLY AND CIRCLE THE NUMBER THAT BEST DESCRIBES YOUR CRAVING *DURING THE PA*

1. During the past week *how often* have you thought about drinking or about how good a drink woul make you feel?
   - **0** Never (0 times during the past week)
   - **1** Rarely (1 to 2 times during the past week)
   - **2** Occasionally (3 to 4 times during the past week)
   - **3** Sometimes (5 to 10 times during the past week or 1 to 2 times per day)
   - **4** Often (11 to 20 times during the past week or 2 to 3 times per day)
   - **5** Most of the time (20 to 40 times during the past week or 3 to 6 times per day)
   - **6** Nearly all of the time (more than 40 times during the past week or more than 6 times per day)
2. At its most severe point, *how strong* was your craving during the past week?
   - **0** None at all
   - **1** Slight, that is a very mild urge
   - **2** Mild urge
   - **3** Moderate urge
   - **4** Strong urge, but easily controlled
   - **5** Strong urge and difficult to control
   - **6** Strong urge and would have drunk alcohol if it were available
3. During the past week *how much time* have you spent thinking about drinking or about how good a drink would make you feel?
   - **0** None at all
   - **1** Less than 20 minutes
   - **2** 21 to 45 minutes
   - **3** 46 to 90 minutes
   - **4** 90 minutes to 3 hours
   - **5** Between 3 to 6 hours
   - **6** More than 6 hours

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CASE SCENARIO

You assess Mr. Smith, a 46-year-old male who endorses a history of daily alcohol usage, up to a “mickey” of vodka per day.

Currently he is experiencing “shaking”, sweating and anxiety. He states he last drank 3 hours ago. He endorses a history of a seizure in the context of alcohol withdrawal 5 years ago.

He denies any past history of “DTs” (Delirium Tremens). When you ask him about hallucinations, he laughs and states he has never seen any “pink elephants”.

How many criteria does he meet for alcohol withdrawal?

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ALCOHOL/SEDATIVE WITHDRAWAL

Withdrawal within several hours to a few days after cessation or reduction of use that has been heavy/prolonged with two or more of the following:

Autonomic hyperactivity (e.g. sweating, pulse greater than 100)

Increased hand tremor

Insomnia

Nausea or vomiting

Transient visual, tactile, or auditory hallucinations or illusions

Psychomotor agitation

Anxiety

Generalized tonic-clonic seizures (3% in alcohol, 20-30% in sedatives)

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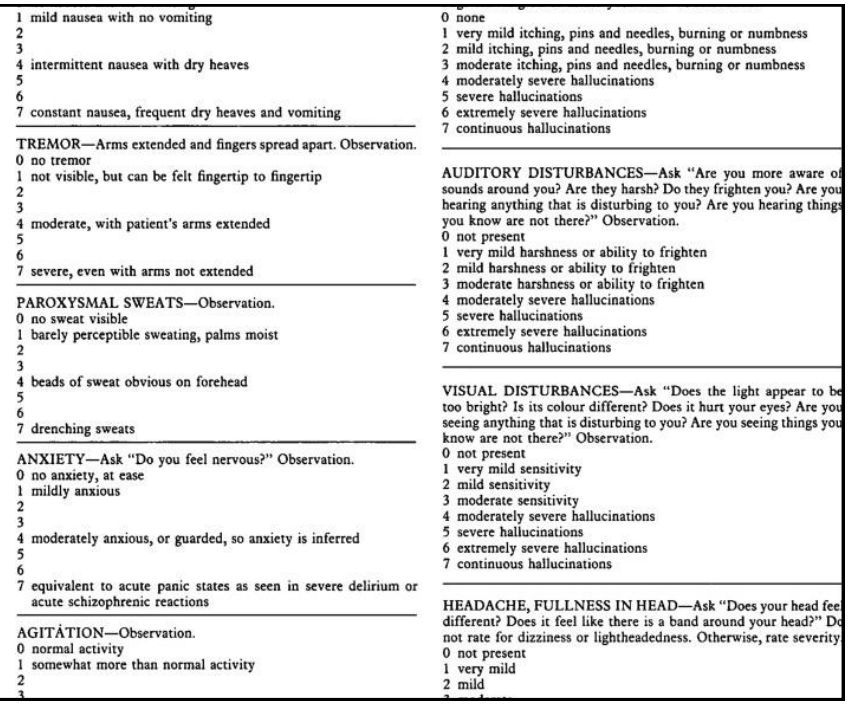
WITHDRAWAL SCALES

Clinical Institute Withdrawal Assessment for Alcohol (CIWA)



1 mild nausea with no vomiting
2
3
4 intermittent nausea with dry heaves
5
6
7 constant nausea, frequent dry heaves and vomiting

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

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

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

AGITATION—Observation.
0 normal activity
1 somewhat more than normal activity
2

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

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

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 hallucinations
5 severe hallucinations
6 extremely severe hallucinations
7 continuous hallucinations

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 lightheadedness. Otherwise, rate severity.
0 not present
1 very mild
2 mild

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WITHDRAWAL SCALES

Prediction of Alcohol Withdrawal Severity Scale (PAWSS) *Maldonado et al., 2014*

Part A: Threshold Criteria: ("+" or "-/-", no point)

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

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

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.

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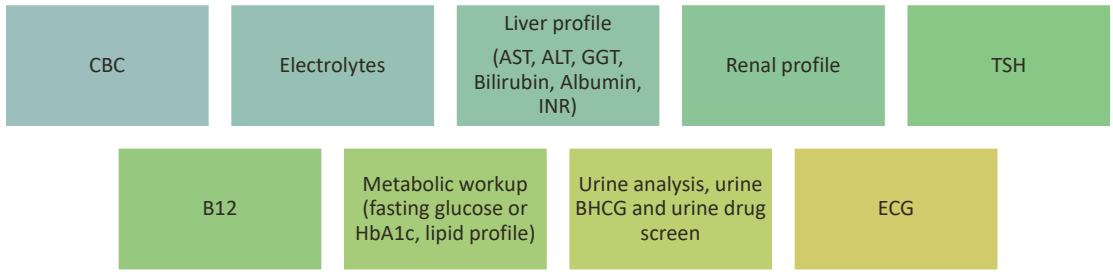

INITIAL INVESTIGATIONS

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ALCOHOL WITHDRAWAL

Indications for outpatient management of alcohol withdrawal:

- Committed to abstinence, willing to start treatment and agrees to not drink while being treated for alcohol withdrawal
- No history of severe withdrawal (seizures, delirium tremens, hospital admissions)
- Not on high doses of opioids or sedating medications, no history of misuse
- Has good supports at home and spouse, relative, or friend agrees to dispense the medication
- Age < 65
- No hepatic decompensation (ascites, encephalopathy), no cirrhosis with liver dysfunction

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GERIATRIC CONSIDERATIONS

Use the Prediction of Alcohol Withdrawal Severity Scale (PAWSS) to screen for those requiring medical withdrawal management (prior delirium, seizures, or protracted withdrawal). Patients who are in poor general health, acutely suicidal, have dementia, are medically unstable, or who need constant one-on-one monitoring should receive 24-hour medical, psychiatric, and/or nursing inpatient care in medically-managed and monitored intensive treatment or hospital settings. [GRADE: Evidence: High; Strength: Strong]

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ALCOHOL WITHDRAWAL

Clinical Institute Withdrawal Assessment for Alcohol, Revised (CIWA-Ar) is the standard monitoring scale with strong evidence of validity

Diazepam remains the first-line medication, given its long half-life and liposoluble properties (great for loading)

Chlordiazepoxide works similarly but is harder to find in hospital formularies today

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 significant liver dysfunction (signs of cirrhosis such as low albumin, high bilirubin/INR)

Other medications have been explored (valproic acid, carbamazepine, clonidine) although there is no major advantage over benzodiazepines

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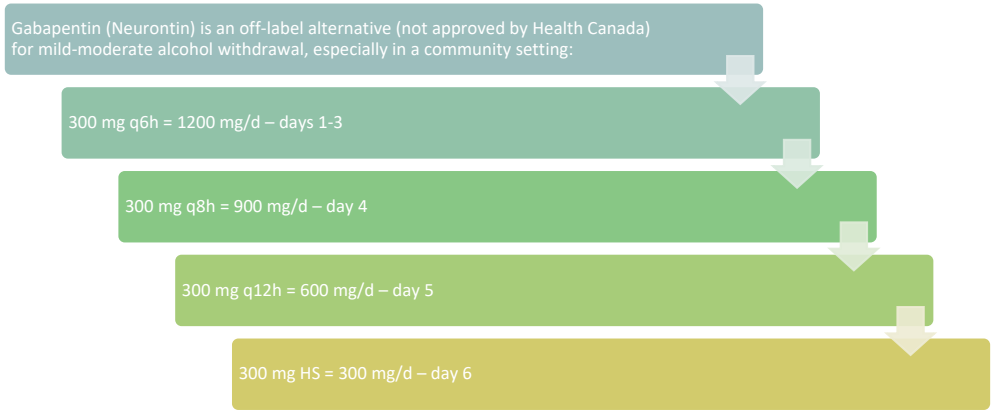
ALCOHOL WITHDRAWAL



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ALCOHOL WITHDRAWAL

Do not forget about thiamine supplementation (100 mg IM x 3 days then 100 mg PO; some experts suggest 250-500 mg daily)

If cannot given IM (ex: outpatient setting), thiamine 100 mg PO TID is recommended as it will help increase likelihood of adequate dose

Geriatric guidelines:

- As a harm reduction strategy for chronic heavy drinkers, it is recommended that at least 50 mg of thiamine supplementation daily be used to prevent Wernicke-Korsakoff syndrome, progressive cognitive decline and increased frailty. [GRADE: Evidence: Low; Strength: Strong]
- To prevent the development of Wernicke's encephalopathy during withdrawal in older adults, at least 200 mg of parenteral thiamine (IM or IV) should be administered daily for 3–5 days. [GRADE: Evidence: Low; Strength: Strong]

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ALCOHOL WITHDRAWAL

If discontinuation is not advisable and/or the patient prefers to avoid medical withdrawal management, a gradual taper (example 25% decrease every week) can be done in the community

As a harm reduction strategy for older adults in controlled environments, where medical withdrawal is not available or deemed appropriate, it is recommended that a managed alcohol taper be considered. Individualize the taper by 1 standard drink every 3 days (aggressive tapering), weekly (moderate tapering), or every 2–3 weeks (mild tapering) with CIWA-Ar monitoring to keep the withdrawal symptom score < 10. The approach should be individualized, incremental, and with an indeterminate timeline.
[Consensus]

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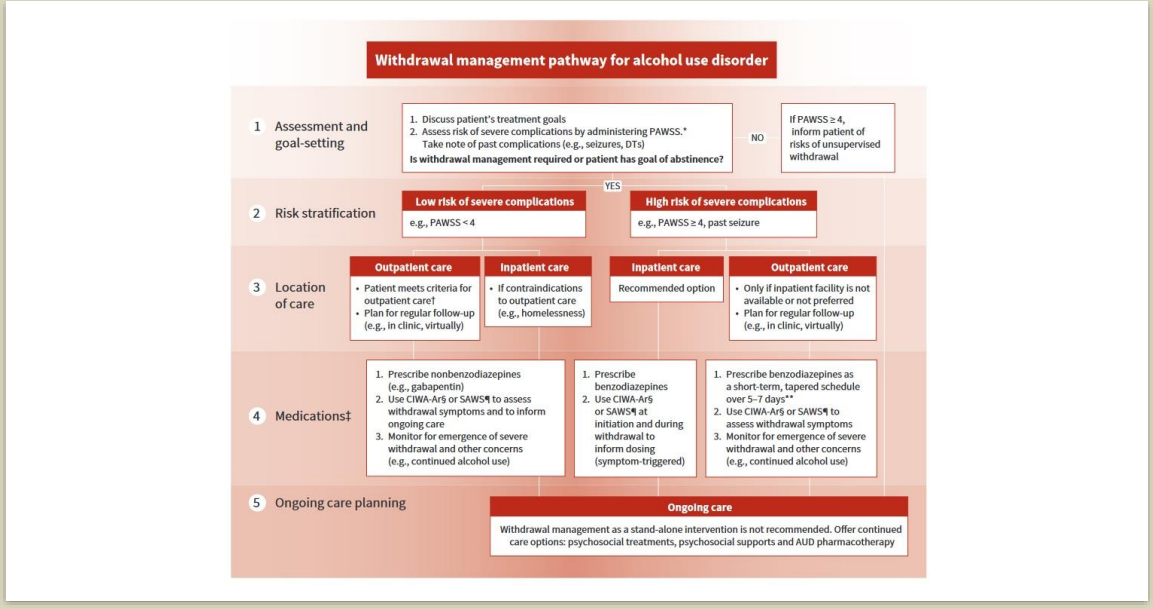

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DOES ANYONE KNOW THE NUMBER NEEDED TO TREAT (NNT) FOR NALTREXONE?

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ANTI-CRAVING THERAPY

Anti-craving medications have strong evidence in Alcohol Use Disorder (Number Needed to Treat 9-10)

Anti-craving is strongly recommended for at least 6-12 months initially, although anti-craving medication may be prescribed for many years and patients can have intermittent periods of therapy

Anti-craving therapy may be safely discontinued when the patient:

- no longer has cravings
- is confident that relapse will not happen if the medication is stopped
- has strong supports in place
- no longer has contact with people who misuse alcohol
- has learned alternative and more adaptive coping strategies

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ANTI-CRAVING SELECTION

Health Canada Indication:

Naltrexone (Revia) – suggested in harm reduction (APA recommended)	H
Acamprosate (Campral) – suggested in abstinence (APA recommended)	R
Disulfiram (Antabuse) – abstinence with good supervision (APA suggested)	H

Preferred Off Label Options:

Topiramate (Topamax) – off label (APA suggested)	R
Gabapentin (Neurontin) – off label (APA suggested)	R

H = Mainly metabolized by the hepatic system
R = Mainly metabolized by the renal system

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NEW CMAJ 2023 GUIDELINES
ANTI-CRAVING SELECTION

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Table 3: Pharmacotherapy for alcohol use disorder*†

	First-line options		Second-line options	
Characteristic	**Naltrexone**	**Acamprosate**	**Topiramate**	**Gabapentin**
Efficacy	NNT to prevent return to heavy drinking is 12 (95% CI 8 to 26)[18] NNT to prevent return to any drinking is 20 (95% CI 11 to 500)[18] Reduced craving (Hedges' g = 0.144 [small effect size], 95% CI 0.045 to 0.244)[19]	NNT to prevent return to any drinking is 12 (95% CI 8 to 26)[18] Increased days abstinent by 11 d (95% CI 5.08 to 16.81)[20]	Decreased heavy drinking days by 9.0% (95% CI −15.3% to −2.7%)[18] Decreased drinking days by 6.5% (95% CI −12.0% to −1.0%)[18] Increased the odds of maintaining abstinence up to 12 mo (OR 1.88, 95% CI 1.06 to 3.34)[21]	Decreased % heavy drinking days (Hedges' g = 0.5478 [medium effect size], 95% CI 0.0145 to 1.0812)[21]
Concurrent alcohol use	Safe to start while using alcohol, but may be more effective after withdrawal management	Safe to start while using alcohol, but may be more effective after withdrawal management	Safe to start while using alcohol	Safe to start while using alcohol, but may be more effective if patients are abstinent for ≥ 3 d
Contra-indications	• Naltrexone hypersensitivity • Any current opioid use (prescribed or nonmedical) • Acute opioid withdrawal • Acute hepatitis or liver failure	• Acamprosate hypersensitivity • Severe renal impairment • Breastfeeding	• Topiramate hypersensitivity • Pregnant or planning pregnancy • Narrow-angle glaucoma • Nephrolithiasis	Gabapentin hypersensitivity
Cautions	• Renal impairment • Severe hepatic impairment • Concomitant use of other potentially hepatotoxic drugs • Pregnancy and breastfeeding† • Youth patients aged < 18 yr†	• Moderate renal impairment • Youth patients aged < 18 yr and older patients aged > 65 yr† • Pregnancy†	• Concomitant use of valproic acid • Conditions or therapies that predispose to acidosis	• Renal impairment • Pregnancy and breastfeeding† • Youth patients aged < 18 yr and older patients aged > 65 yr† • Concomitant use of opioids and other central nervous system depressants • Compromised respiratory function • Neurological disease or cognitive impairment
Adverse effects	Nausea, headache and dizziness Starting at low dose or abstinence can reduce adverse effects	Diarrhea, vomiting and abdominal pain	Psychomotor slowing, difficulty concentrating, speech or language problems, somnolence, fatigue and mood disturbance Starting at low dose and titrating up can reduce adverse effects	Ataxia, slurred speech and drowsiness
Dosing	Start: 25 mg OD for 3 d Titrate: to 50 mg OD over 2 wk as tolerated	2 × 333 mg tablets TID	Titrate: to 2 × 50 mg tablets BID over several weeks as tolerated	Start: at 100–300 mg TID Titrate: PRN to 1800 mg max daily

Note: BID = twice daily, CI = confidence interval, NNT = number needed to treat, OD = once daily, OR = odds ratio, PRN = as needed or when necessary, TID = 3 times daily.
*There are limited data to support combination pharmacotherapy. Single-medication trials are suggested at first. Suggested duration is 6 months or longer. We gathered information for contraindications, cautions, adverse effects and dosage from the cited clinical trials and Health Canada–approved product monographs.
†Safety and efficacy have not been well established in these patient populations. Careful assessment of benefit and risks, fully informed patient consent and more frequent monitoring are advised.

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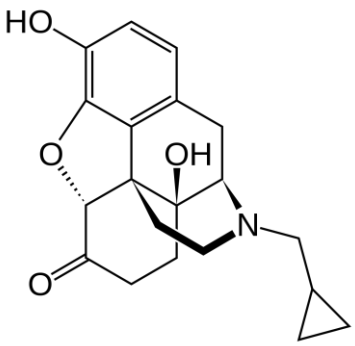
NALTREXONE (LU 532)



Brand name: Revia

Availability: PO in Canada, monthly IM in US

Dosage: 25 mg daily for 2 days then 50 mg daily, please increase to 100-150 mg daily if no response and well tolerated

Metabolism: mainly hepatic; no meal required

Mechanism of action: competitive opioid antagonist, blocks the pleasurable effects of alcohol

Pregnancy category: C

Important drug-drug interactions: no opioid for 1-3 days (monograph says 7-10 days) before initiation as it will block the analgesic effects and can precipitate withdrawal

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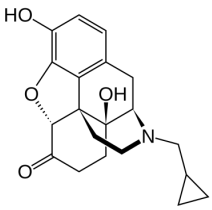
NALTREXONE (LU 532)



Potential adverse effects:

- Nausea (10%)
- Depression (5 to 7%)
- Fatigue (4%)
- Anxiety (2%)
- Headache (7%)
- Dizziness (4%)
- Insomnia (3%)
- Sleepiness (2%)
- Eosinophilic pneumonia
- Reversible elevation in transaminases (contraindicated in acute hepatitis and liver failure)

Monitoring:

- Pre-initiation liver panel (at minimum AST, ALT and bilirubin) and urine drug screen
- Start naltrexone if transaminases are not more than 5 times the normal level or GGT > 500, caution is warranted if transaminases are 3 – 5 times normal or GGT 300 – 500 (it is agreed among AUD experts that the risk of ongoing drinking far outweighs theoretical risk of further liver damage in patients with cirrhosis)
- Repeat liver panel at 3 months (some say 1 month)

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ACAMPROSATE (LU 531)

Brand name: Campral

Availability: PO

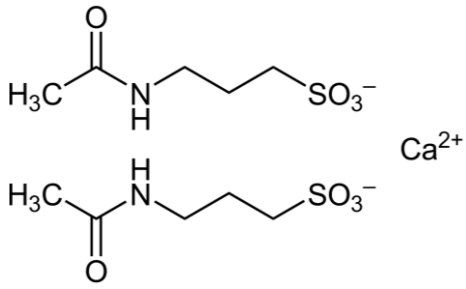
Dosage: 333 mg TID for 2 days then 666 mg TID

Metabolism: mainly renal; no meal required

Mechanism of action: by modulating glutamate and increasing GABA, which has been disturbed by regular, heavy drinking (this imbalance and discomfort makes some people return to drinking); it can mitigate alcohol withdrawal symptoms

Pregnancy category: C

Important drug-drug interactions: none



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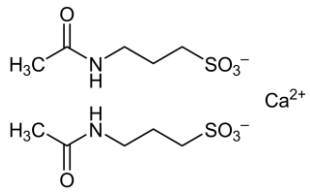
ACAMPROSATE (LU 531)



Potential adverse effects:

- Mild diarrhea or loose stools
- Nausea
- Anxiety
- Depression

Monitoring:

- Pre-initiation renal panel (if moderate renal impairment, use 333 mg TID only, contraindicated in severe renal impairment)
- No other tests required although consider monitoring renal function over time

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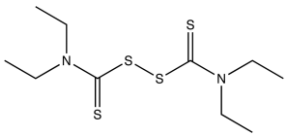
DISULFIRAM



Brand name: Antabuse

Availability: PO at compounding pharmacies

Dosage: Classical regimen is 500 mg for 2 weeks then 250 mg daily although most clinicians start at 125 mg daily (range 125-500 mg daily)

Metabolism: mainly hepatic; no meal required

Mechanism of action: deters alcohol use by inhibiting the enzyme acetaldehyde dehydrogenase and making the person sick when they drink; need to wait 24-48 hours after last alcohol use before starting

Pregnancy category: C

Important drug-drug interactions: patient should wear a medical alert bracelet as medications can contain alcohol; disulfiram is a 2C9 inhibitor

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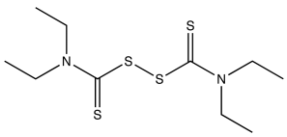
DISULFIRAM



Potential adverse effects:

- Drowsiness
- Headache
- Garlic-like smell
- Anxiety
- Hepatotoxicity
- Metallic taste
- Fatigue
- Rash, acne
- Depression, psychosis (rare)
- Peripheral neuropathy (prolonged use)
- You can explain that if the person drinks, he or she might become warm and red, and experience dizziness, a throbbing headache, nausea and a pounding heart
- You can instruct them to avoid anything with alcohol (many vitamin tonics, cough and cold remedies, mouthwashes and some candies contain alcohol)
- It is generally OK to use cosmetic preparations that contain alcohol, such as aftershave lotions on the face, but test a small area beforehand

Monitoring:

- Pre-initiation liver panel, renal panel, CBC and electrolytes
- Repeat liver panel after 2 weeks and periodically thereafter

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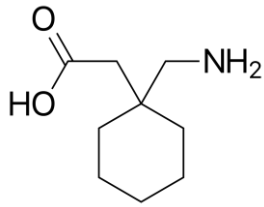
GABAPENTIN



Brand name: Neurontin

Availability: PO

Dosage: Start at 300 mg BID or TID, can go to 600 mg TID or higher based on response and tolerability

Metabolism: renal; no meal required

Mechanism of action: by increasing GABA biosynthesis and by modulating dopamine, can be used to manage alcohol withdrawal as well as cravings

Pregnancy category: C

Important drug-drug interactions: avoid with other CNS depressants

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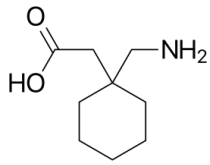
GABAPENTIN



Potential adverse effects:

- Dizziness
- Sedation
- Weight gain
- Nausea and vomiting
- Peripheral edema
- Rash (including risk of SJS)
- Withdrawal symptoms if abrupt discontinuation
- Ataxia
- Nervousness
- Depression
- Nystagmus
- Tremor
- Rhabdomyolysis

Monitoring:

- Pre-initiation renal panel
- Consider repeating renal panel periodically
- Cut dose if renal impairment

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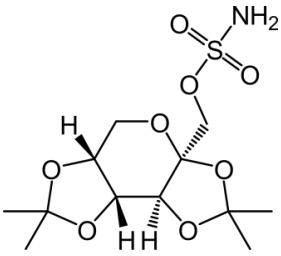
TOPIRAMATE



Brand name: Topamax

Availability: PO

Dosage: 25 mg – 150 mg BID (increase by 25 mg increments every 3-7 days)

Metabolism: major renal and minor hepatic; no meal required

Mechanism of action: unknown, likely by inhibiting the release of glutamate and potentiating the activity of GABA, also may improve mood and sleep

Pregnancy category: D

Important drug-drug interactions: weak 3A4 inducer and can decrease oral contraceptive levels

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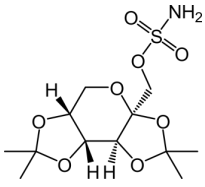
TOPIRAMATE



Potential adverse effects:

- Skin numbness or tingling (51%)
- Taste disturbance (23%)
- Loss of appetite (20%)
- Difficulty with concentration (15%)
- Difficulty with memory (13%)
- Diarrhea (12%)
- Itching (10%)
- Indigestion (9%)
- Sinusitis (8%)
- Metabolic acidosis
- Secondary narrow angle-closure glaucoma
- Headache (24%)
- Fatigue (22%)
- Insomnia (19%)
- Nervousness (14%)
- Drowsiness (12%)
- Dizziness (12%)
- Nausea (10%)
- Flu-like symptoms (9%)
- Muscle pain (8%)
- Kidney stones

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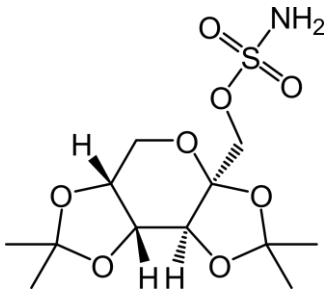
TOPIRAMATE

Monitoring:

- Pre-initiation electrolytes with serum bicarbonate, liver panel and renal panel
- Cut dose in half in renal impairment
- Ongoing monitoring of electrolytes and serum bicarbonate recommended



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ANTI-CRAVING SELECTION

Ondansetron (off-label)	• May be useful for early-onset AUD (< 25 years), patients having a severe, destructive history of AUD, ?related to deficiency of serotonin transport system
Varenicline (off-label)	• Controlled trials suggest varenicline reduces drinking when given to cigarette smokers who also drink heavily
Baclofen (off-label)	• High-dose baclofen not found to be effective in large RCT
Medication combinations	• Controlled trials indicate combinations may work better than monotherapy (example: naltrexone + gabapentin)

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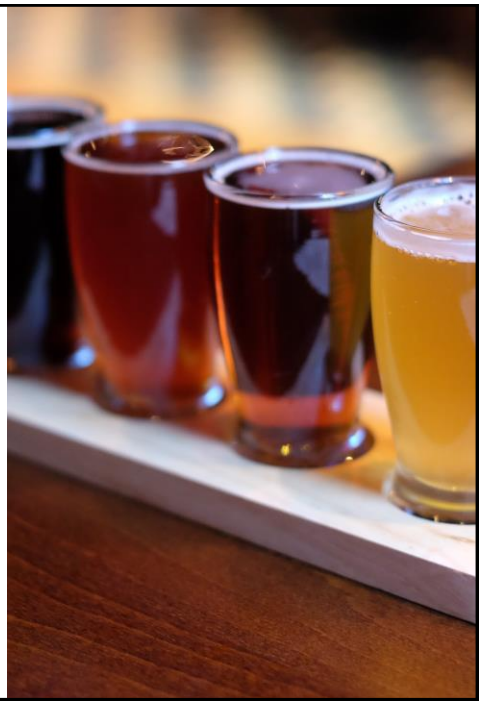
COMORBID AUD + OUD

Preferred option is likely buprenorphine (over naltrexone)

Some patients drink alcohol in part for relief of opioid withdrawal symptoms

Relieving opioid withdrawal will reduce alcohol consumption

Gabapentin is another option however gabapentin increases risk of opioid overdose



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CONCURRENT TREATMENT

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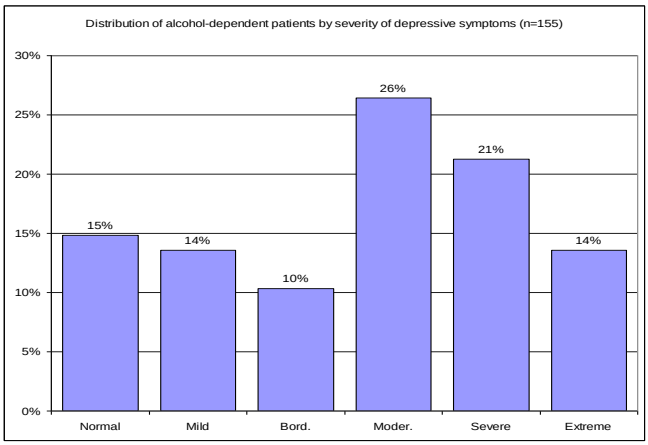
Majority (85%) of alcohol-dependent patients have depressive symptoms

Severity of depressive symptoms in 61% of alcohol-dependent patients is moderate or higher



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DA VINCI (DEPRESSION AND ALCOHOLISM – VALIDATION OF AN INTEGRATED CARE INITIATIVE)

Rationale for the integrated pathway:

- High prevalence of both disorders
- High comorbidity between two conditions
- Established causal links between MDD and AUD
- Undertreatment of MDD in patients with AUD and AUD in patients with MDD
- Low treatment retention and poor treatment outcomes

DA VINCI demonstrated:

- Effectiveness of combined use of anti-craving medications and antidepressants
- Effectiveness of combined psychotherapy (CBT in DA VINCI) and pharmacotherapy

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CHOOSING WISELY CANADA

"Don't routinely prescribe antidepressants as first-line treatment for depression comorbid with an active alcohol use disorder without first considering the possibility of a period of sobriety and subsequent reassessment for the persistence of depressive symptoms."

"The concurrent management of psychiatric illness and alcohol use disorders requires evaluation of the role alcohol plays as a causative factor for depressive symptoms. Studies have found that response rates to antidepressants are higher when antidepressants are reserved for persistence of symptoms after a period of sobriety lasting from two to four weeks. Additionally, studies have demonstrated remission from depressive symptoms with sobriety in the absence of antidepressant treatment in a significant percentage of cases. Management of comorbid psychiatric illness and substance use disorders including alcohol dependence involves assessment and treatment delivered in a concurrent manner."

(One of their references is research from the DA VINCI project where integrated antidepressant and anti-craving therapy was used)

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SCREENING

Major Depressive Disorder

Patient Health Questionnaire (PHQ-9) is great for screening

Quick Inventory of Depressive Symptomatology (QIDS) is great for monitoring and is free to use

Hamilton Depression Rating Scale (HAM-D) and Montgomery and Asberg Depression Rating Scale (MADRS) are often used in studies but need to be purchased

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AUD + MDD

First-line for Major Depressive Disorder (MDD)

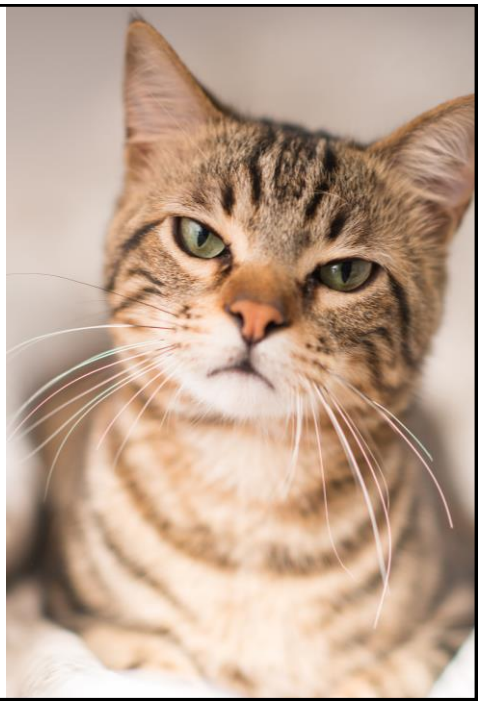
Sertraline (Zoloft) 25 – 200 mg AM

Venlafaxine XR (Effexor XR) 37.5 – 375 mg AM

Fluoxetine (Prozac)10 – 80 mg AM

Mirtazapine (Remeron)15 – 60 mg HS

*Bupropion (Wellbutrin) is usually not recommended due to the seizure risk



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Antidepressant therapy should be continued up to 12 months post-remission

Some patients may require indefinite antidepressant therapy

If possible refrain from combining antidepressants or augmenting with other agents in AUD unless they have maintained abstinence for 3-6 months and have ongoing significant depressive symptoms

Avoid the use of benzodiazepines for treating anxiety or depression in patients with AUD, due to the risk of misuse and respiratory depression

In the case of non-restorative sleep where other causes (such as sleep apnea) have been ruled out, melatonin 6 mg HS or trazodone 50-100 mg HS can be used first

AUD + MDD

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AUD + ANXIETY DISORDER

Three combinations have more evidence of benefit for improving anxiety and drinking outcomes:

Naltrexone + sertraline

- Improves both outcomes
- Sertraline is a well tolerated SSRI overall (low risk of weight gain, sedation or sexual dysfunction)

Gabapentinoids (pregabalin, gabapentin)

- Pregabalin may work faster for anxiety (3-4 days) and is First-line for Social Anxiety Disorder (SAD) and Generalized Anxiety Disorder (GAD)
- Gabapentin has greater evidence of benefit for AUD

Buspirone

- Although evidence is more limited than the first two options