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CADTH Reference List

Guidelines for Treatment of Alcohol Withdrawal in Outpatient Settings

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Summary of Abstracts

CADTH

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Key Message

We found 5 evidence-based guidelines about the treatment of alcohol withdrawal in outpatient settings.

Research Question

What are the evidence-based guidelines regarding the treatment of alcohol withdrawal in outpatient settings?

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, the Cochrane Database of Systematic Reviews, the International HTA Database, and the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concept was alcohol withdrawal. A CADTH-developed search filter was applied to limit retrieval to guidelines. Where possible, retrieval was limited to the human population. The search was completed on September 13, 2022, and limited to English-language documents published since January 1, 2017. Internet links were provided, where available.

Selection Criteria and Summary Methods

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria presented in Table 1. Full texts of study publications were not reviewed. The overall summary of findings was based on information available in the abstracts of selected publications. Open-access, full-text versions of evidence-based guidelines were reviewed when available, and relevant recommendations were summarized.

Results

Five evidence-based guidelines were identified regarding the treatment of alcohol withdrawal in outpatient settings.[1-5]

A reference of potential interest that did not meet the inclusion criteria due to unclear methodology but provided guidance and recommendations regarding the treatment of alcohol withdrawal in outpatient settings is summarized in Appendix 1. Additional references of potential interest that did not meet the inclusion criteria are provided in Appendix 2.

Table 1: Selection Criteria

Criteria	Description
Population	People with alcohol dependence commencing treatment for alcohol withdrawal in an outpatient setting
Intervention	Any treatment for alcohol withdrawal
Comparator	Not applicable
Outcomes	Recommendations regarding the treatment of alcohol withdrawal (e.g., which treatments are recommended, guidance for specific population groups)
Study designs	Evidence-based guidelines

Overall Summary of Findings

Five evidence-based guidelines were identified regarding the treatment of alcohol withdrawal in outpatient settings.[1-5] For patients with mild withdrawal, 3 guidelines[3-5] recommend using carbamazepine and gabapentin for treatment. The British Columbia Centre on Substance Use (2019) also recommends treating patients at low risk of severe complications with clonidine.[5] For patients with moderate to severe withdrawal symptoms, 2 guidelines[3,4] recommend using benzodiazepines as first-line therapy, with carbamazepine,[3,4] gabapentin,[3,4] valproate,[3] or phenobarbital[4] as potential adjunctive or alternative therapies.

One guideline[4] also recommends valproic acid, alpha-2 adrenergic agonists, or beta adrenergic antagonists as adjuncts to benzodiazepines for varying symptoms. However, the American Society of Addiction Medicine (2020) recommends against using clonidine alone to treat prevent or treat withdrawal-related seizures or delirium.[4] In addition, 1 guideline[4] recommends supportive care as a component of ambulatory withdrawal treatment.

Recommendations for benzodiazepine administration are symptom-triggered therapy,[2,4] fixed-dosing or fixed-schedule therapy,[1,2,4] and front-loading therapy.[4] The recommendation for gabapentin administration is fixed-schedule therapy.[2] One guideline[4] also recommends strategies for the safe use of benzodiazepines and specifies inappropriate medications for the treatment of alcohol withdrawal. A detailed summary of guideline recommendations can be found in Table 2.

Table 2: Summary of Recommendations in Included Guidelines

Guideline development group (year)	Summary of recommendations
Haber et.al (2021)[1]	"Diazepam should be administered in a fixed dose regimen in ambulatory settings, or for those with concomitant medical, psychiatric or substance use disorders." (p. 123) *Grade of recommendation: C (body of evidence provides some support for recommendation but care should be taken in its application)*
Institut national d'excellence en santé et en services sociaux (2021)[2]	**Recommendations for administering benzodiazepines:** • **Symptom-triggered therapy:** "One dose is taken at the time intervals indicated on the individual prescription if the person has at least one withdrawal symptom." (p. 3) • **Fixed-schedule therapy:** "One dose is taken at the time intervals specified on the individual prescription." (p. 3) **Recommendations for administering gabapentin:** • **Fixed-schedule therapy with additional PRN doses:** "Regular dosing is done at the time intervals indicated on the individual prescription. An additional dose is taken at the indicated time intervals if the person has at least one sign or symptom: anxiety, tremor, irritability, strong alcohol cravings, or night-time insomnia." (p. 3)
Tiglao et.al (2021)[3]	**Recommendations for treating mild withdrawal:** • "Carbamazepine (Tegretol) and gabapentin (Neurontin) are appropriate options for treating mild AWS." • *Evidence rating: C (consensus, disease-oriented evidence, usual practice, expert opinion, or case series)* **Recommendations for treating moderate withdrawal:** • "Benzodiazepines are the preferred medication for treating moderate AWS." • *Evidence rating: A (consistent, good-quality, patient-oriented evidence)* **Recommendations for adjuncts to benzodiazepines:** • "Gabapentin, carbamazepine, and valproate (Depacon) may be prescribed as adjuncts to benzodiazepines if symptoms persist despite adequate benzodiazepine use." • *Evidence rating: C (consensus, disease-oriented evidence, usual practice, expert opinion, or case series)*

Guideline development group (year)	Summary of recommendations
American Society of Addiction Medicine (2020)[4]	Further details on the recommendations found in this guideline can be found within the resource. **Recommendations for supportive care:** • "Supportive care is a critical component of alcohol withdrawal management. Providers should ensure patients are educated about what to expect over the course of withdrawal, including common signs and symptoms and how they will be treated." (p. 7 and 35) • Educate patients/caregivers about monitoring withdrawal severity and creating an appropriate home environment. (p. 7 and 35) • "Patients should be advised to drink non-caffeinated fluids and that a daily multivitamin may be beneficial." (p. 7 and 35) • "Patients can be offered oral thiamine. Typical dosing is 100 mg PO per day for 3–5 days." (p. 7 and 35) • "Clinicians must explain the importance of taking medications as prescribed and confirm the patient's understanding." (p. 7 and 35) • "Communicate that safe alcohol withdrawal management may necessitate a transfer to a more intensive level of care including to an inpatient setting and secure the patient's agreement to transfer if there are indications that management in the ambulatory setting is not safe or effective." (p. 7 and 35 to 36) **Recommendations for treating patients at risk of developing new or worsening symptoms:** "Patients at risk of developing new or worsening signs or symptoms of withdrawal while away from the ambulatory treatment setting should be provided with pharmacotherapy.(…)Benzodiazepines, carbamazepine, or gabapentin are all appropriate options for monotherapy. Providing at least a single dose of benzodiazepine followed by ongoing treatment according to symptom severity is also appropriate." (p. 8 and 36 to 37) **Recommendations for treating mild withdrawal:** • Patients at minimal risk of developing severe or complicated alcohol withdrawal or complications of alcohol withdrawal may be provided pharmacotherapy or supportive care alone. (p. 8 and 37) • "If providing medication, carbamazepine or gabapentin are appropriate options." (p. 8 and 37) **Recommendations for treating moderate withdrawal:** "Benzodiazepines are first-line treatment. Carbamazepine or gabapentin are appropriate alternatives. For patients with a contraindication for benzodiazepine use, carbamazepine, gabapentin, or phenobarbital (in Level 2-WM settings for providers experienced with its use) are appropriate. Carbamazepine, gabapentin, or valproic acid (if no liver disease or childbearing potential) may be used as an adjunct to benzodiazepines." (p. 8 to 9 and 38) **Recommendations for treating severe but not complicated withdrawal:** "Benzodiazepines are first-line treatment. Phenobarbital is an appropriate alternative for providers experienced with its use. For patients with a contraindication for benzodiazepine use, phenobarbital, carbamazepine, or gabapentin are appropriate. The use of adjunct medications is also appropriate." (p. 8 and 38)

Guideline development group (year)	Summary of recommendations
	Recommendations for treating severe or complicated withdrawal: "In a Level 2-WM ambulatory setting (e.g., with extensive monitoring), phenobarbital monotherapy (managed by a clinician experienced with its use) is an appropriate alternative to benzodiazepines for patients who are experiencing severe alcohol withdrawal or who are at risk of developing severe or complicated alcohol withdrawal or complication of alcohol withdrawal." (p. 9 and 42) **Recommendations for treating uncontrolled symptoms:** "If a patient is taking medication as prescribed and symptoms are not controlled as expected: First, consider increasing the dose; if over-sedation or inadequate monitoring is a concern: • Reassess for appropriate level of care • Consider switching medications • If using benzodiazepines, consider adding an adjunct medication" (p. 8 and 38) **Recommendations for benzodiazepine use:** • "Longer-acting benzodiazepines are the preferred agents." (p. 8 and 39) • "If waiting for lab test results or if the test(s) are unavailable, if a patient has signs of significant liver disease, use a benzodiazepine with less hepatic metabolization." (p. 8 and 39) • "Clinicians should monitor patients taking benzodiazepines for signs of over-sedation and respiratory depression." (p. 8 and 39) • "A benzodiazepine prescription to treat alcohol withdrawal should be discontinued following treatment." (p. 8 and 39) • To manage benzodiazepine misuse or diversion risk, clinicians can dispense or prescribe the minimum amount necessary. Alternative medications can also be considered, such as carbamazepine or gabapentin. (p. 8 and 39) • "Benzodiazepines should not be prescribed to patients with a history of even mild adverse events with benzodiazepine.(…) Benzodiazepines can be used with caution in patients with a high risk of benzodiazepine diversion including patients with a current or past benzodiazepine use disorder for the short period of acute alcohol withdrawal." (p. 8 and 39) • Patients and their caregivers should be educated about risks relevant to benzodiazepine use. (p. 8 and 39) **Recommendations for administering benzodiazepines:** • Symptom-triggered therapy: ◦ "At short-term observational settings with continuous monitoring (e.g., Level 2-WM), symptom-triggered treatment conducted by trained staff is the preferred benzodiazepine dosing method." (p. 8 and 40) "At settings without extended on-site monitoring (Level 1-WM), symptom-triggered dosing is appropriate if patients or a caregiver can reliably monitor signs and symptoms with a withdrawal severity scale and follow dosing guidance." (p. 8 and 40)

Guideline development group (year)	Summary of recommendations
	• Front-loading and/or fixed-dosing therapy: ◦ "At short-term observational settings with continuous monitoring (e.g., Level 2-WM)… (f)ront loading while under clinical supervision or fixed dosing with additional as-needed medication is appropriate." (p. 8 and 40) ◦ At settings without extended onsite monitoring (Level 1-WM), if patients or a caregiver cannot reliably monitor signs and symptoms with a withdrawal severity scale or follow dosing guidance, front loading while under clinical supervision or fixed dosing with additional as-needed medication is appropriate. (p. 8 to 9 and 40) ◦ "Front loading is recommended for patients experiencing severe alcohol withdrawal (e.g., CIWA-Ar ≥ 19). Diazepam and chlordiazepoxide are preferred agents for front loading." (p. 8 and 40) ◦ "When using a fixed-dose schedule, patients' signs and symptoms should still be monitored. A few additional take-home doses can be provided to take as needed. When initiating a fixed-dose regimen, arrange for the patient to be follow up with the following day to modify the dose if needed." (p. 9 and 40) ◦ "If prescribing a shorter-acting benzodiazepine, using a fixed-dose regimen with a gradual taper may be appropriate to reduce the likelihood of breakthrough and rebound signs and symptoms." (p. 9 and 40) **Recommendations for gabapentin use:** "Gabapentin is a favorable choice for treating alcohol withdrawal when a clinician also plans to use it for a patient's ongoing treatment of alcohol use disorder." (p. 9 and 41) **Insufficient evidence for valproic acid as monotherapy:** "There is insufficient evidence to support the use of valproic acid as monotherapy for the treatment of alcohol withdrawal." (p. 9 and 41 to 42) **Recommendations for A2AAs and beta-adrenergic antagonist use:** • "Alpha2-adrenergic agonists (A2AAs) such as clonidine can be used as an adjunct to benzodiazepine therapy to control autonomic hyperactivity and anxiety when symptoms are not controlled by benzodiazepines alone. They should not be used alone to prevent or treat withdrawal-related seizures or delirium." (p. 9 and 42) • "Beta-adrenergic antagonists (beta-blockers) can be used as an adjunct to benzodiazepines in select patients for control of persistent hypertension or tachycardia when these signs are not controlled by benzodiazepines alone. They should not be used to prevent or treat alcohol withdrawal seizures." (p. 9 and 42) • **Inappropriate medications:** Oral or IV alcohol, baclofen, and magnesium are inappropriate medications for the treatment of alcohol withdrawal. (p. 9 and 42 to 43)
British Columbia Centre on Substance Use (2019)[5]	"Clinicians should consider non-benzodiazepine medications, such as carbamazepine, gabapentin, or clonidine, for outpatient withdrawal management in patients at low risk of severe complications of alcohol withdrawal." (p. 57) *Quality of evidence: moderate; strength of recommendation: strong*

A2AA = Alpha2-adrenergic agonist; AWS = alcohol withdrawal syndrome; CIWA-Ar = the Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised; PO = per os (by mouth); PRN = pro re nata (as needed); WM = withdrawal management.

References

Guidelines and Recommendations

1. Haber P, Riordan BC. Guidelines for the treatment of alcohol problems. 4th ed. Sydney (AU): University of Sydney; 2021: https://alcoholtreatmentguidelines.com.au/pdf/guidelines-for-the-treatment-of-alcohol-problems.pdf. Accessed 2022 Sep 19. *See: Recommendation 8.28 (page 123)*

2. Administration of benzodiazepines or gabapentin prescribed via an individual prescription for alcohol withdrawal. *(Québec's national medical protocol)*. Québec (QC): INESSS; 2021: https://www.inesss.qc.ca/fileadmin/doc/INESSS/Ordonnances_collectives/Sevrage/INESSS_Withdrawal_alcohol_NMP.pdf. Accessed 2022 Sep 19. *See: 2.3 Administering drugs, Outpatient withdrawal (page 3)*

3. Tiglao SM, Meisenheimer ES, Oh RC. Alcohol withdrawal syndrome: outpatient management. *Am Fam Physician*. 2021 Sep 1;104(3):253-262. . PubMed

4. The ASAM clinical practice guideline on alcohol withdrawal management. Rockville (MD): American Society of Addiction Medicine. 2020: https://www.asam.org/docs/default-source/quality-science/the_asam_clinical_practice_guideline_on_alcohol-1.pdf?sfvrsn=ba255c2_2. Accessed 2022 Sep 19. *See: Recommendations IV.6 - IV.11 Supportive care (pages 7 and 35); Recommendations IV.15 - IV.44 Pharmacotherapy (pages 7-9 and 36-43)*

5. Provincial guideline for the clinical management of high-risk drinking and alcohol use disorder. Vancouver (BC): British Columbia Centre on Substance Use (BCCSU); 2019: https://www.bccsu.ca/wp-content/uploads/2021/01/AUD-Guideline.pdf. Accessed 2022 Sep 19. *See: Recommendation 6 (page 57)*

Appendix 1: Summary of Identified Recommendations

Note that this appendix has not been copy-edited.

Best Practice Advocacy Centre New Zealand (bpac^{nz}) (2018) provides recommendations regarding the treatment of alcohol withdrawal in outpatient settings. However, methods used to develop recommendations were unclear. Bpac^{nz} (2018) recommends interventions for use during the first week of alcohol withdrawal, including oral thiamine hydrochloride to prevent Wernicke's encephalopathy and a short course of diazepam to reduce withdrawal symptoms. However, bpac^{nz} (2018) mentions that patients treated with diazepam should be warned of the risks of respiratory depression if they resume alcohol consumption. bpac^{nz} (2018) recommends longer term use of multivitamins containing B and folic acid if needed. Further, bpac^{nz} (2018) recommends using disulfiram as an adjunct to psychological approaches to assist patients with abstinence. bpac^{nz} (2018) also provides recommendations regarding the use of topiramate for people without mental health issues.

Guidelines and Recommendations

Unclear Methodology

Assessment and management of alcohol misuse by primary care. Dunedin (NZ): bpacnz; 2018: https://bpac.org.nz/2018/alcohol.aspx. Accessed 2022 Sep 19 *See: Managing alcohol withdrawal in primary care (page 8), Medicines that can be initiated in primary care (page 8-9)*

Appendix 2: Additional References

Note that this appendix has not been copy-edited.

Guidelines and Recommendations

Not Specific to Outpatient Setting

VA/DoD clinical practice guideline for the management of substance use disorders. *Version 4.0*. Washington (DC): U.S. Department of Veterans Affairs; 2021: https://www.healthquality.va.gov/guidelines/MH/sud/VADoDSUDCPG.pdf. Accessed 2022 Sep 19. *See: Recommendation 5 (page 40) and Recommendation 6 (page 42)*

Practice guideline for the pharmacological treatment of patients with alcohol use disorder. Washington (DC): American Psychiatric Association; 2017: https://psychiatryonline.org/doi/pdf/10.1176/appi.books.9781615371969 Accessed 2022 Sep 19. *See: Statement 13 (page 36) and Statement 14 (page 37)*

Alcohol-use disorders: diagnosis and management of physical complications. *NICE Clinical guideline [CG100]*. London (UK): National Institute for Health and Care Excellence (NICE); 2010; updated 2017: https://www.nice.org.uk/guidance/cg100. Accessed 2022 Sep 19. *See: 1.1.3 Treatment for acute alcohol withdrawal (page 6)*