

CADTH Health Technology Review

Treatment Programs for Substance Use Disorder

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Abbreviations

ASAM	American Society of Addiction Medicine
AUD	alcohol use disorder
AWS	alcohol withdrawal syndrome
CCSMH	Canadian Coalition for Seniors' Mental Health
CUD	cannabis use disorder
MAP	managed alcohol program
RCT	randomized controlled trial
RT	residential treatment
SR	systematic review
SUD	substance use disorder

Key Messages

- Moderate to weak evidence suggests that patients with substance use disorders who received residential treatment were more likely than outpatients to complete treatment and be considered abstinent. Comparisons between residential treatment and outpatient programs for other outcomes were unclear.
- Strong- to weak-quality evidence showed that residential treatment services for patients with substance use disorders was effective in improving various outcomes including substance use, social, criminal activity, and mental health outcomes. However, residential treatment was likely associated with poorest survival outcomes after discharge compared to other treatments.
- Managed alcohol programs in hospital settings appeared to be effective and safe in preventing and treating alcohol withdrawal syndrome in surgical patients, trauma patients, or hospitalized patients. The level of evidence was not assessed.
- There was evidence that managed alcohol programs in community settings improved drinking patterns, alcohol-related harm, criminal activity, mental health, and social and physical well-being. The level of evidence was not assessed.
- The American Society of Addiction Medicine clinical practice guideline provides recommendations for the identification and management of alcohol withdrawal in inpatient and ambulatory settings. Patients' current signs and symptoms, levels of risk for developing severe or complicated withdrawal or complications of withdrawal, and other dimensions should be taken into consideration in the assessment process to determine the appropriate level of care. Strength of recommendations was not assessed.
- The Canadian Coalition for Seniors' Mental Health recommends that patients with cannabis use disorder should be considered for residential treatment if they are unable to effectively reduce or cease their cannabis use (level of evidence: Low; strength of recommendation: Strong).

Context and Policy Issues

According to the National Indicators Report using data of more than 200,000 Canadian adults aged in their mid-to-late 30's seeking community-based treatment services from 2016 to 2018, 68% individuals reported alcohol as the most common substance use disorder (SUD), followed by cocaine and cannabis.¹ More than half of the individuals had at least 2 SUDs.¹ Males were the predominant gender for substance abuse compared to females (62% versus 38%).¹

SUD treatment programs are generally divided into 2 categories: inpatient or outpatient programs.² Inpatient treatment may be part of a hospital program or may occur at a special clinic that requires patients to stay in the facility with 24-hour medical and emotional support.² The treatment in inpatient programs is more intensive and is designed to treat serious addiction, and the duration of treatment varies from 28 days to 6 months.² On the other hand, patients treated in the outpatient programs typically stay at home and come to the facility during the day, maintaining their normal daily routines.² Outpatient treatment occurs in hospital clinics, mental health clinics, counsellor's offices, or local health unit offices.³ The treatment in outpatient programs is suitable for patients with mild to moderate addiction and the duration of treatment varies from 3 months to more than a year.² Depending on

the patient's condition and the level of care requirement, the patient can attend a standard outpatient treatment (1 or 2 group therapy sessions a week) or an intensive outpatient treatment (10 to 20 hours of counselling or group therapy spread over 3 days a week).³ The outpatient programs are more affordable but usually have a lower success rate compared to inpatient programs.²

A recent CADTH report⁴ published in 2017 examined the clinical effectiveness of inpatient and outpatient treatment programs in adults with SUD and found some evidence regarding the comparative treatment between inpatient and outpatient programs for alcohol and substance use problems. Because of limitations of the included studies, no strong conclusions could be made.⁴

The aim of this report is to review the comparative clinical effectiveness of inpatient and outpatient programs, as well as the clinical effectiveness of each program for treatment of SUD, regardless of comparators. The report also reviews evidence-based guidelines regarding treatment programs for SUD.

Research Questions

1. What is the comparative clinical effectiveness of inpatient treatment programs versus outpatient treatment programs for SUD?
2. What is the clinical effectiveness of treatment programs for the treatment of SUD?
3. What are the evidence-based guidelines regarding treatment programs for individuals with SUD?

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE and PsycINFO through Ovid, the Cochrane Database of Systematic Reviews, the international HTA database, 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 search concepts were substance use disorders and 1 of inpatient or outpatient treatment programs mentioned. Search filters were applied to limit retrieval to health technology assessments, systematic reviews (SRs), meta-analyses, network meta-analyses, and guidelines. For question 1, a second search was conducted for randomized controlled trials (RCTs), controlled clinical trials, and any other type of clinical trial. For this part, search terms had to be in a major subject heading or the article title, and both inpatient and outpatient treatment programs were required to be mentioned. Where possible, retrieval was limited to the human population. The search was also limited to English-language documents published between January 1, 2016 and April 26, 2021.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published before 2016. Primary studies retrieved by the search were excluded if they were included in the previous CADTH report.⁴ Guidelines with unclear methodology were also excluded.

Critical Appraisal of Individual Studies

The included publications were critically appraised by 1 reviewer using the following tools as a guide: A Measurement Tool to Assess systematic Reviews 2 (AMSTAR 2)⁵ for SRs and the Appraisal of Guidelines for Research & Evaluation (AGREE) II instrument⁶ for guidelines. Summary scores were not calculated for the included studies; rather, the strengths and limitations of each included publication were described narratively.

Table 1: Selection Criteria

Criteria	Description
Population	Individuals diagnosed with SUD, alone or in combination with a comorbid psychiatric disorder or chronic pain Eligible SUDs: alcohol dependence, opioid use disorder, cocaine use disorder, and cannabis use disorder Eligible psychiatric disorders: post-traumatic stress disorder, depression, major depressive disorder, anxiety, sleep disorders, bipolar disorder, borderline personality disorder, eating disorder
Intervention	Q1: Treatment programs for SUD delivered in an inpatient setting Q2 and Q3: Treatment programs for SUD delivered in an inpatient or outpatient setting
Comparator	Q1: Treatment programs for SUD delivered in an outpatient setting Q2: An alternative treatment program for SUD Usual care (e.g., pharmacological therapy) No treatment (e.g., pre-post) Virtual programs for SUD Q3: Not applicable
Outcomes	Q1 and Q2: Clinical benefits (e.g., detoxification completion rate, abstinence, health-related quality of life), and harms (e.g., hallucinations, suicidality, seizures) Q3: Recommendations regarding best practices (e.g., guidance regarding best treatment program(s) by condition, contraindications)
Study Designs	Q1: HTA, SR, RCT, NRS Q2: HTA, SR

HTA = health technology assessment; NRS = non-randomized study; RCT = randomized controlled trial; SR = systematic review; SUD = substance use disorder.

Summary of Evidence

Quantity of Research Available

A total of 463 citations were identified in the literature search. Following the screening of titles and abstracts, 426 citations were excluded and 37 potentially relevant reports from the electronic search were retrieved for full-text review. One potentially relevant publication was retrieved from the grey literature search for full-text review. Of these potentially relevant articles, 34 publications were excluded for various reasons and 4 publications met the inclusion criteria and were included in this report. These comprised 2 SRs and 2 guidelines. Appendix 1 presents the PRISMA⁷ flow chart of the study selection. Additional references of potential interest are provided in Appendix 5.

Summary of Study Characteristics

Additional details regarding the characteristics of included SRs^{8,9} (Table 2) and ASAM⁸ American Society of Addiction Medicine clinical practice guideline¹⁰ and the Canadian Coalition for Seniors' Mental Health (CCSMH) guideline¹¹ (Table 3) are provided in Appendix 2.

Study Design

Both included SRs^{8,9} conducted a narrative synthesis on inpatient and outpatient programs for the treatment of SUDs. One SR by de Andrade et al.⁸ included all evidence except SRs and case report study designs, and the other SR by Brooks et al.⁹ included all evidence regardless of study design. Both SRs performed literature searches from multiple databases.

The included ASAM guideline¹⁰ was developed for the identification and management of patients with alcohol withdrawal in both inpatient and ambulatory settings. Evidence was systematically searched from major databases and websites with a predefined search. The quality of the included literature was rated and draft guideline statements were developed by the consultant and reviewed by the committee members. Each statement was judged by committee members using a 9-point Likert scale. Agreement was reached by consensus after several face-to-face meetings. The strength of the recommendation was not provided.

The CCSMH guideline¹¹ was developed for the prevention, identification, assessment, and treatment of cannabis use disorder (CUD). Evidence was systematically searched from main databases. Relevant literature was reviewed by guideline development working group members. All recommendations were voted on and more than 75% agreement was required for a recommendation to be adopted. Members discussed the recommendations until they reached 100% consensus on each recommendation. The Grading of Recommendations, Assessment Development and Evaluation – GRADE – was used to assess the strength of recommendations (strong, weak) based on the quality of evidence (high, medium, low).

Country of Origin

The included SRs were conducted by authors from Australia⁸ and Canada.⁹ The included guidelines were conducted by authors from the US¹⁰ and Canada.¹¹

Patient Population

The SR by Brooks et al.⁹ included studies of patients specifically diagnosed with alcohol use disorder (AUD) and the other SR by de Andrade et al.⁸ included studies involving patients with

SUD. Details of patient characteristics were not fully reported in both SRs. Sample sizes varied considerably and ranged from 29 to 53,017 in 1 SR⁸ and from 1 to 200 in the other SR.⁹

The target populations in the ASAM guideline¹⁰ are patients with alcohol withdrawal syndrome (AWS) including those with medical conditions, those who take opioids, and those who are pregnant. The intended users of the ASAM guideline¹⁰ are physicians, nurse practitioners, physician assistants, and pharmacists who provide alcohol withdrawal management in specialty and non-specialty addiction treatment settings.

The target populations in the CCSMH guideline¹¹ are older adults (born between 1946 and 1964) with CUD, as well as their caregivers and families; the intended users are clinicians who provide treatment for patients with CUD.

Interventions and Comparators

The SR by de Andrade et al.⁸ compared residential treatment (RT) programs for individuals with SUD with other treatment types including outpatient treatment, pharmacotherapy detoxification, and RT programs with different adjunctive therapies. The RT programs provided intensive care and support for individuals with severe and complex SUD (including alcohol and other drug withdrawal or maintenance management in a hospital or supervised residential facility), individual and group psychological support, mutual self-help and peer therapeutic communities, and support reintegration into the community.⁸

The SR by Brooks et al.⁹ compared managed alcohol programs (MAPs) in hospital settings for patients with severe AUD with other treatments or placebo. Uncontrolled studies such as prospective interventional studies, retrospective chart reviews, and case studies were also examined in the SR. MAPs administered regular doses of beverage alcohol or IV alcohol to people with AUD, alongside related health and social supports.⁹ The SR also examined the effectiveness of MAPs in community settings.

The ASAM guideline¹⁰ considered multi-step programs in alcohol withdrawal management in inpatient and ambulatory settings. The CCSMH guideline¹¹ considered various approaches in the management and treatment of CUD.

Outcomes

The outcomes considered in the included SRs^{8,9} were substance use, social and mental health outcomes, criminal activity, and safety outcomes. One SR⁸ reported follow-up periods, which varied significantly among included studies (i.e., 3 months to 11 years). The other SR⁹ did not report follow-up periods of the included studies.

The ASAM clinical practice guideline¹⁰ considered the clinical effectiveness and safety outcomes of alcohol withdrawal management in inpatient and ambulatory settings. The CCSMH guideline¹¹ considered the effectiveness and safety outcomes of the management and treatment procedures of CUD.

Summary of Critical Appraisal

The details of the quality assessment of the SRs^{8,9} (Table 3) are provided in Appendix 3.

Both included SRs^{8,9} were explicit in their objectives and inclusion criteria for the review, and in their selection of the study design for inclusion. Both also included a comprehensive literature search strategy. None of the SRs reported whether a protocol had been published before

the conducting of the review. One SR⁸ did not report whether study selection was performed in duplicate and the other SR⁹ did not report whether data extraction was performed in duplicate. The quality of the included studies was assessed in 1 SR⁸ and not in the other.⁹ Both SRs^{8,9} did not report the sources of funding of the studies included in their review and did not provide a list of excluded studies. Both SRs^{8,9} narratively synthesized the findings of the included studies without performing meta-analysis. Conflicts of interest were declared in both SRs.^{8,9} Overall, the included SRs were of low methodological quality.

Both included guidelines^{10,11} were explicit in scope and purpose (i.e., objectives, health questions, and populations), and had a clear presentation (i.e., specific and unambiguous recommendations, different options for management of the condition or health issue, and easy to find key recommendations). Regarding stakeholder involvement, both guidelines clearly defined target users and the development groups; however, it was unclear if the views and preferences of the patients were sought. For rigour of development, both guidelines reported details of systematic searches for evidence, criteria for selecting evidence, and methods of formulating the recommendations. The guidelines considered health benefits, side effects, and risks in formulating the recommendations; were peer-reviewed before publication; and provided a procedure for updating. However, only 1 guideline¹¹ assessed and reported the strength of its recommendations. For applicability, the guidelines were explicit in the facilitators and barriers to application, advice and/or tools on how the recommendations can be put into practice, resource implications, and monitoring and or auditing criteria. For editorial independence, both guidelines reported that the funding bodies had no influence on the content of the guidelines. The competing interests of the guideline development group members were reported. Overall, both guidelines were of high methodological quality.

Summary of Findings

The main findings and authors' conclusions of the SRs (Table 6) are presented in Appendix 4.

Comparative Clinical Effectiveness of Inpatient Treatment Programs Versus Outpatient Treatment Programs for SUD

The evidence regarding the comparative clinical effectiveness of inpatient treatment programs versus outpatient treatment programs for SUD was found from 1 SR.⁸

The SR by de Andrade et al.⁸ included 1 study of weak quality comparing outpatient treatment to RT for treatment completion and abstinence rates at discharge and found that a significantly higher proportion of SUD patients receiving RT completed treatment and considered abstinence compared to outpatient clients. The SR⁸ included 2 studies comparing 3 types of treatment (i.e., RT, community pharmacotherapy, and inpatient detoxification). One study of moderate quality found that RT was associated with significant improvements in heroin abstinence, criminal activity, mental health, and physical health. The other study of strong quality found that RT had no significant impact on the number of offences committed. The SR⁸ also included 1 study of weak quality reporting no significant differences among 3 types of treatments (i.e., RT, therapeutic community, and maintenance therapy) in scores of mental health or quality of life.

Clinical Effectiveness of Treatment Programs for the Treatment of SUD

Evidence on the effectiveness of inpatient programs for SUD was derived from 2 SRs that examined the clinical effectiveness and safety of RT programs⁸ and MAP in hospital settings.⁹ One SR also examined the clinical effectiveness and safety of MAP in community settings.

Substance Use Outcomes

Out of 17 studies (7 strong, 5 moderate, and 5 weak quality) reporting substance use outcomes included in the SR by de Andrade et al.⁸ 16 showed a statistically significant positive effect in substance use outcomes over time following RT. One study showed inconclusive results.

The SR by Brooks et al.⁹ included 6 controlled studies that compared MAP with other treatments (e.g., alternative AWS treatment drug) or placebos for treating or preventing AWS. Three studies found that MAP was effective in treating or preventing AWS, 2 studies found that MAP was noninferior to the alternative treatments, and 1 study was inconclusive. The SR⁹ included 3 uncontrolled studies: 2 studies found improvements in AWS when alcohol was used to treat AWS in trauma and burn patients, and 1 study found variations in alcohol elimination rates in alcohol-dependent patients. The SR⁹ included 2 retrospective chart reviews: 1 retrospective chart review found that patients had been inconsistently and inappropriately treated with alcohol and only 10% were referred to addiction treatment and another retrospective chart review found no significant difference in the Clinical Institute Withdrawal Assessment for Alcohol Scale scores between the alcohol group (beer or 50% distilled alcohol) and the benzodiazepine group for the treatment of AWS. Of 5 case studies included in the SR, 4 reported successful alcohol administration to treat AWS in hospital patients. The SR by Brooks et al.⁹ included 4 SRs that provided mixed evidence. Two SRs published in 2013 reported evidence supporting the use of alcohol in preventing but not treating AWS. Two older SRs published in 1997 and 2004 found a lack of evidence to support the use of alcohol to treat or prevent AWS. The SR by Brooks et al.⁹ also included 5 cross-sectional surveys of hospital administrators (4 in the US and 1 in the UK) that found evidence that IV alcohol and beverage alcohol were prescribed to treat and prevent AWS.

The SR by Brooks et al.⁹ included 14 studies reporting the effectiveness of MAP in community settings. Of the 14 studies, 2 pre-post studies of MAP, 5 case studies, and 2 non-randomized controlled studies (the authors did not indicate which control interventions were used) found that MAP was associated with decreased consumption of alcohol and reduced rates of hospitalization and detox admission.

Mental Health Outcomes

The SR by de Andrade et al.⁸ included 17 studies (7 strong, 5 moderate, and 5 weak quality) reporting on mental health outcomes. Sixteen studies showed a significant positive effect in mental health outcomes following RT, such as psychological distress, post-traumatic stress disorder, depression, anxiety, stress, and general mental health over time. One study showed no significant difference between RT groups with different adjunctive therapies in depression symptoms.

The SR by Brooks et al.⁹ provided evidence from preliminary results of 2 grey literature articles and a non-peer-reviewed article that MAP in community settings was associated with positive mental health outcomes.

Social Outcomes

The SR by de Andrade et al.⁸ included 11 studies (3 strong, 4 moderate, and 4 weak quality) that reported on social outcomes. Ten studies reported a significant positive effect on social outcomes including quality of life, satisfaction, employment, family, and social relationships after RT treatment, while 1 study showed unclear results.

The SR by Brooks et al.⁹ included 2 pre-post studies, 2 grey literature articles, and a non-peer-reviewed article reporting that MAP in community settings was associated with positive social outcomes including housing stability and compliance with medical care.

Criminal Activity Outcomes

The SR by de Andrade et al.⁸ included 9 studies (2 strong, 3 moderate, and 4 weak quality) that reported on criminal activity outcomes. Eight studies reported a significant positive effect on criminal activity outcomes after RT treatment. One study showed significant reductions in recorded offences following inpatient detoxification and community-based pharmacotherapy programs but not RT.

The SR by Brooks et al.⁹ included 2 pre-post studies, 5 case studies, and 2 non-randomized controlled studies reporting that MAP in community settings was associated with decreased rates of incarcerations, decrease use of crisis services, and more positive interaction with police.

Safety

The SR by de Andrade et al.⁸ included 1 strong-quality study examining the relationship between treatment type and mortality. The study found that SUD patients discharged from residential withdrawal (detoxification) services were associated with highest risk of death followed by residential rehabilitation compared to counselling and other treatments in the first year post-treatment.

The 3 2-arm comparison studies included in the SR by Brooks et al.⁹ concluded that alcohol is a safe and viable option to manage AWS in surgical patients (IV alcohol), trauma patients (IV alcohol), and hospitalized patients (beverage alcohol).

Guidelines

The ASAM guideline¹⁰ was developed for the identification and management of patients with AWS in both inpatient and ambulatory settings. Its clinical practice recommendations include the identification and diagnosis of alcohol withdrawal signs and symptoms, initial assessment of patients, level of care determination, management of signs and symptoms, addressing complications, and special settings and populations. Details of the recommendations for the identification and management are clearly provided in each section of the guideline. The management is divided into 2 broad categories: ambulatory and inpatient settings. For the general approach in the level of care determination, the guideline suggests that patients' current signs and symptoms, levels of risk for developing severe or complicated withdrawal or complications of withdrawal, and other dimensions should be taken into consideration when choosing the program of treatment. The guideline suggests that patients with AWS who have limited risk factors could safely be managed in an ambulatory setting. Those with active risk of suicide should be managed in an inpatient psychiatric setting. Patients should be transferred from an ambulatory setting to a more intensive care or inpatient setting when they have unresolved agitation or severe tremor and more severe and persistent signs and symptoms (e.g., vomiting, agitation, hallucination, confusion, or seizure), when they worsen in existing medical or psychiatric conditions, and when there are signs of over-sedation and evidence of a return to alcohol use, and when they experience syncope or have unstable vital signs.

The CCSMH guideline¹¹ recommends that accredited RT should be considered for patients unable to effectively reduce or cease their cannabis use (level of evidence: Low; strength of recommendation: Strong)

Limitations

There was limited evidence regarding the comparative clinical effectiveness of inpatient treatment programs versus outpatient treatment programs for SUD. One identified SR⁸ included moderate- to weak-quality studies comparing outpatient treatment to RT for SUD. Two SRs that were identified to provide evidence on the effectiveness of programs for SUD⁸ and AUD⁹ in inpatient settings had several limitations. The SR by de Andrade et al.⁸ assessed the quality of the included studies and found that the quality of many studies was affected by high attrition rates and methodological shortcomings. The quality of the studies was not assessed in the SR by Brooks et al.⁹ Overall, many studies included in the SRs had small sample sizes, used self-reported data only, and were of weak study designs (e.g., case series, grey literature articles, and non-peer-reviewed articles). The intervention was heterogeneous regarding the core treatment components, method of component delivery, the number and length of sessions, and the length of follow-up. Patient characteristics and type of SUD also greatly varied among included primary studies.

There were no significant methodological limitations of both included guidelines^{10,11} except that the strength of recommendations in the ASAM guideline¹⁰ was not graded.

Conclusions and Implications for Decision- or Policy-Making

This report identified 2 narrative SRs.^{8,9} One SR⁸ reported weak to moderate evidence for the comparative clinical effectiveness of inpatient RT programs versus outpatient treatment for SUD and assessed the effectiveness of RT programs, in general, for individuals with SUD. The other SR⁹ examined the effectiveness of MAP for the prevention and treatment of AWS in hospital and community settings.

Weak to moderate evidence suggests that SUD patients who received RT were more likely than outpatients to complete treatment and be considered abstinent, as judged by the physicians. Regarding the clinical effectiveness of RT across several SUDs, strong- to weak-quality evidence showed that RT was effective in improving various outcomes including substance use, social and criminal activity, and mental health outcomes. However, RT was likely associated with a high risk of death after treatment. Most studies reporting the effectiveness of MAP through the administration of alcohol to hospital inpatients provided positive outcomes related to the prevention and treatment of AWS in inpatient settings. MAP appeared to be safe to manage AWS in surgical, trauma, or hospitalized patients. Evidence from community MAP studies also suggests that community-based MAPs improved drinking patterns, alcohol-related harm, criminal activity, mental health, and social and physical well-being. Evidence on the comparative clinical effectiveness between inpatient and outpatient settings of MAPs was not identified.

The ASAM guideline¹⁰ provides recommendations for the identification and management of patients with AWS in medical settings including inpatient and outpatient settings. Patient's

current signs and symptoms, level of risk for developing severe or complicated withdrawal or complications of withdrawal, and other dimensions should be considered before determining which program is most suitable to treat alcohol withdrawal. The CCSMH guideline¹¹ recommends that RT should be considered for hard to treat patients with CUD.

The previous CADTH report⁴ included 1 narrative SR, 1 RCT, 1 longitudinal study, and 1 retrospective study. The SR included 2 comparative studies with a follow-up of 1 month and 2 months reporting that participants who underwent community detoxification were more likely to be drinking less or had more abstinence compared to those undergoing facility-based detoxification. The RCT with a follow-up of up to 18 months found that initial inpatient treatment for alcohol detoxification was significantly better in the abstinence group compared to outpatient treatment; however, the benefit of the inpatient treatment reduced over time. The longitudinal study found that inpatient clients (hospital or other residential) consumed less alcohol after 1-year treatment than outpatient clients. The study also found that inpatient clients had significantly greater engagement with Alcoholics Anonymous attendance, which was likely the mediator for the relationship between treatment type and alcoholic consumption. And lastly, the included retrospective study showed that participants in the RT treatment program for SUD (alcohol, cocaine, marijuana, opioids, methamphetamines) were more than 3 times as likely to complete treatment as compared to those in the outpatient treatment settings. Thus, findings in this report extend those in the previous CADTH report⁴ showing that clients undergoing inpatient treatment for SUD including alcohol problems were more likely to complete treatment and considered abstinence compared to outpatient clients.

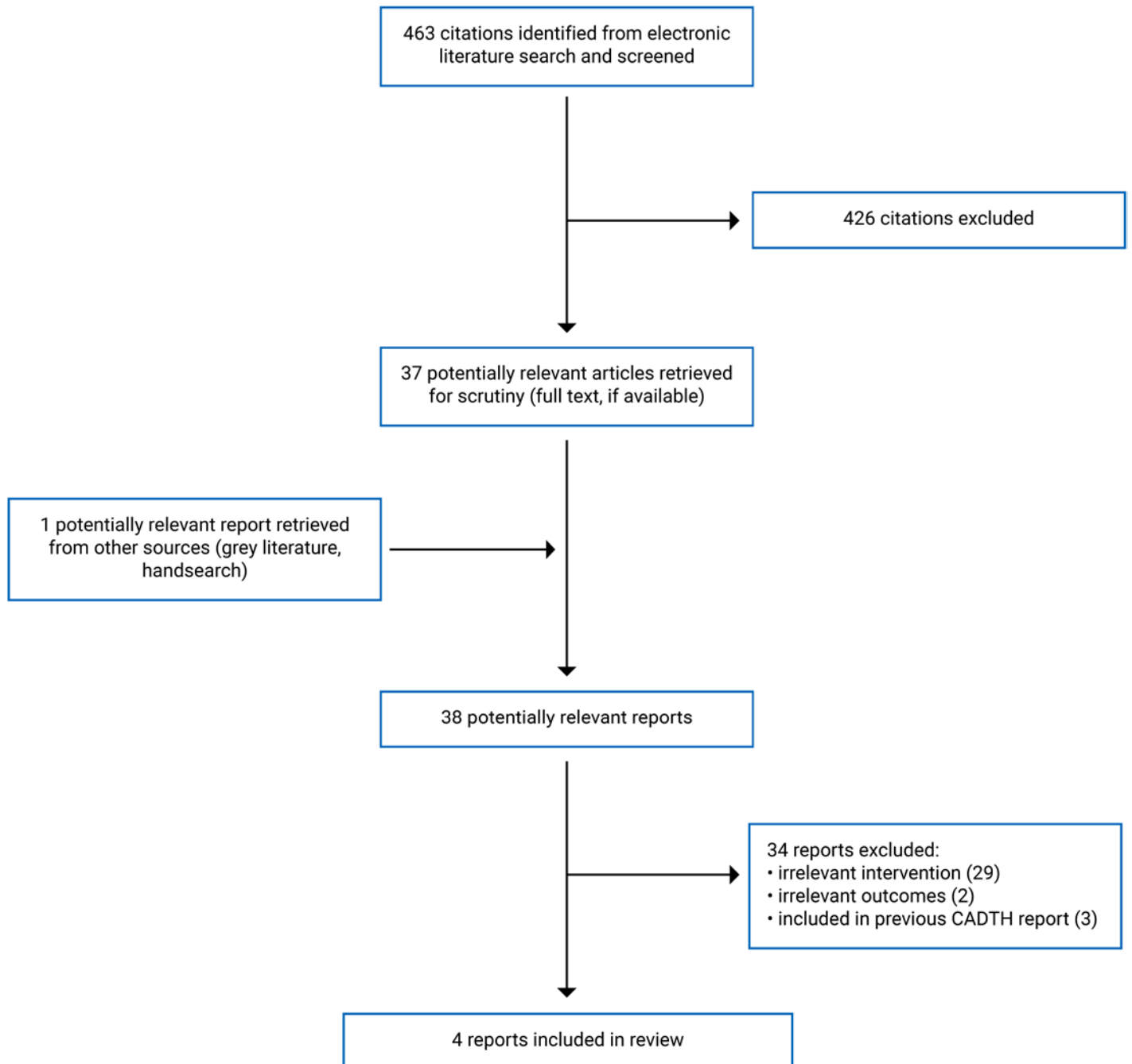
Taken together, there is some evidence regarding the comparative clinical effectiveness of inpatient treatment programs versus outpatient treatment programs for SUD. A number of studies included in the identified SRs provided some evidence on the clinical effectiveness of RT programs for the treatment of SUD,⁸ and MAP for the treatment and prevention of AWS in hospital settings and in community settings.⁹ However, the limitations of the studies — mainly attrition from research follow-ups and methodological shortcomings — preclude a conclusive conclusion and limit the generalizability of the results. The positive outcomes described after RT and MAP should be therefore interpreted with caution. There is a strong need to conduct high-quality research in treatment programs for SUD delivered in inpatient and outpatient settings; the comparative results could impact policy-making and translate to practice.

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Appendix 1: Selection of Included Studies

Figure 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of Included Systematic Reviews

Study citation, country, funding	Objectives, primary studies, quality assessment tool, databases, and analysis	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
<p>de Andrade et al. (2019)⁸ Australia Funding: Nothing declared</p>	<p>Objectives: to provide an update on the evidence base for the residential treatment of SUD to identify the most effective model of care, their core components, and promising directions for future research and clinical practice</p> <p>Total: 23 studies</p> <p>Quality assessment tool: EPHPP Quality Assessment Tool for Quantitative Studies</p> <p>Databases: Medline, CINAHL, PsycARTICLES and PsycINFO. From January 1, 2013 to December 31, 2018</p> <p>Analysis: narrative synthesis</p>	<p>Patients with SUD</p> <p>Sample size: 29 to 53,017</p> <p>Mean age: varied; not all studies reported age of participants</p> <p>Gender: both male and female; not all studies reported gender</p>	<p>Intervention: RTPs</p> <p>Comparators: other treatment types</p>	<p>Outcomes:</p> <ul style="list-style-type: none"> • substance use • social • criminal activity • mental health • mortality <p>• Follow-up: 3 months to 11 years</p>
<p>Brooks et al. (2018)⁹ Canada Funding: NR</p>	<p>Objectives: To characterize the current literature on the provision of alcohol of MAPs in community and hospital settings</p> <p>Total: 42 studies (28 hospital studies, 14 community studies); 6 literature reviews, 10 case studies, 2 chart reviews, 6 uncontrolled studies, 4 2-group comparison studies, 9 controlled studies, 5 surveys</p> <p>Quality assessment tool: No</p> <p>Databases: Medline, Embase, PsycInfo, and EBSCO CINAHL Plus; and 10 grey literature repositories. Not report on date of search</p> <p>Analysis: Narrative synthesis</p>	<p>People with severe AUDs</p> <p>Sample size: 1 to 200</p> <p>Mean age: 23 to 75 years</p>	<p>Intervention: MAP (administration of controlled doses of beverage alcohol to prevent withdrawal and stabilize drinking patterns)</p> <p>Comparators: other treatments or placebo</p>	<p>Outcomes:</p> <ul style="list-style-type: none"> • inpatient – treating or preventing AWS • outpatient – drinking patterns, alcohol-related harms, non-judgmental health, and social care <p>• Follow-up: NR</p>

ACT = assertive community treatment; AUD = alcohol use disorder; AWS = alcohol withdrawing syndrome; EPHPP = Effective Public Health Practice Project; MAP = managed alcohol program; NR = not reported; RTP = residential treatment program; SUD = substance use disorder.

Table 3: Characteristics of Included Guidelines

Intended users, target population	Intervention and practice considered	Major outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
ASAM, Lindsay et al. (2020)¹⁰						
Intended users: physicians, nurse practitioners, physician assistants, and pharmacists who provide alcohol withdrawal management in specialty and non-specialty addiction treatment settings Target population: Patients with AUD	Alcohol withdrawal management in both inpatient and outpatient settings	Appropriate treatment practices for the management of patients with alcohol withdrawal in medical settings	Evidence was systematically searched from main databases and websites for the periods January 2012 to October 2017 A clear description of evidence selection and synthesis was provided	The quality of the included literature was rated using standardized scales	Guideline statements were developed and reviewed based on the literature available. Each statement was judged by committee members using a 9-point Likert scale. Agreement was reached by consensus after several face-to-face meetings	Published in peer-reviewed journal
CCSMH, Bertram et al. (2020)¹¹						
Intended users: clinicians who provide treatment for patients with CUD Target population: older patients with CUD, caregivers and families	Prevention, identification, assessment, and treatment of CUD	Appropriate treatment practices for the management of patients with CUD	Evidence was systematically searched from main databases A clear description of evidence selection and synthesis was provided	GRADE was used to assess the strength of recommendations ^a based on the quality of the evidence ^b	Relevant literature was reviewed by the guideline development working group members. All recommendations were voted, and more than 75% need be reached for a recommendation to be adopted. Members discussed until they reached 100% consensus on each recommendation	Published in peer-reviewed journal

ASAM = American Society of Addiction Medicine; AUD = alcohol use disorder; CCSMH = Canadian Coalition for Seniors' Mental Health; CUD = cannabis use disorder; GRADE = Grading of Recommendations Assessment, Development and Evaluation.

^aStrength of Recommendation: "Strong" indicates a high confidence that desirable consequences of the proposed course of action outweigh the undesirable consequences (or vice versa). "Weak" indicates that there a close balance between benefits and downsides (including adverse effects, and burden of treatment), uncertainty regarding the magnitude of benefits and downsides, uncertainty or great variability in patients' values and preferences, or that the cost or burden of the proposed intervention may not be justified

^bQuality of evidence: "High" = further research is unlikely to change confidence in the estimate of effects. "Medium" = further research is likely to have an important impact on the confidence in the estimate of effect and may change the estimate. "Low" = further research is very likely to have an important impact on the confidence in the estimate of effect and may change the estimate.

Appendix 3: Critical Appraisal of Included Publications

Table 4: Strengths and Limitations of Systematic Reviews Using AMSTAR 2⁵

Item	de Andrade et al. (2019) ⁸	Brooks et al. (2018) ⁹
1. Did the research questions and inclusion criteria for the review include the components of PICO?	Yes	Yes
2. Did the report of the review contain an explicit statement that the review methods were established before the conduct of the review and did the report justify any significant deviations from the protocol?	No	No
3. Did the review authors explain their selection of the study designs for inclusion in the review?	Yes – all research except SR	Yes – all research regardless of study design
4. Did the review authors use a comprehensive literature search strategy?	Yes	Yes
5. Did the review authors perform study selection in duplicate?	Unclear – NR	Yes
6. Did the review authors perform data extraction in duplicate?	Unclear – NR	Unclear – NR
7. Did the review authors provide a list of excluded studies and justify the exclusions?	No	No
8. Did the review authors describe the included studies in adequate detail?	Yes	Yes
9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?	Yes	No
10. Did the review authors report on the sources of funding for the studies included in the review?	No	No
11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	NA – narrative review	NA – narrative review
12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	NA – narrative review	NA – narrative review
13. Did the review authors account for RoB in individual studies when interpreting/discussing the results of the review?	Yes	No
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	Yes	Yes
15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	NA – narrative review	NA – narrative review
16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	Yes	Yes

AMSTAR 2 = A MeaSurement Tool to Assess systematic Reviews 2; NA = not applicable; NR = not reported; PICO = Population, Intervention, Comparator, Outcomes; RoB = risk of bias; SR = systematic review.

Table 5: Strengths and Limitations of Guidelines Using AGREE II⁶

Item	ASAM, Lindsay et al. (2020) ¹⁰	CCSMH, Bertram et al. (2020) ¹¹
Domain 1: Scope and Purpose		
1. The overall objective(s) of the guideline is (are) specifically described.	Yes	Yes
2. The health question(s) covered by the guideline is (are) specifically described.	Yes	Yes
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	Yes	Yes
Domain 2: Stakeholder Involvement		
4. The guideline development group includes individuals from all relevant professional groups.	Yes	Yes
5. The views and preferences of the target population (patients, public, etc.) have been sought.	Unclear	Unclear
6. The target users of the guideline are clearly defined.	Yes	Yes
Domain 3: Rigour of Development		
7. Systematic methods were used to search for evidence.	Yes	Yes
8. The criteria for selecting the evidence are clearly described.	Yes	Yes
9. The strengths and limitations of the body of evidence are clearly described.	Yes	Yes
10. The methods for formulating the recommendations are clearly described.	Yes	Yes
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	Yes	Yes
12. There is an explicit link between the recommendations and the supporting evidence.	Yes	Yes
13. The guideline has been externally reviewed by experts before its publication.	Yes	Yes
14. A procedure for updating the guideline is provided.	Yes	Yes
Domain 4: Clarity of Presentation		
15. The recommendations are specific and unambiguous.	Yes	Yes
16. The different options for management of the condition or health issue are clearly presented.	Yes	Yes
17. Key recommendations are easily identifiable.	Yes	Yes
Domain 5: Applicability		
18. The guideline describes facilitators and barriers to its application.	Yes	Yes
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	Yes	Yes
20. The potential resource implications of applying the recommendations have been considered.	Yes	Yes
21. The guideline presents monitoring and/or auditing criteria.	Yes	Yes

Item	ASAM, Lindsay et al. (2020) ¹⁰	CCSMH, Bertram et al. (2020) ¹¹
Domain 6: Editorial Independence		
22. The views of the funding body have not influenced the content of the guideline.	Yes	Yes
23. Competing interests of guideline development group members have been recorded and addressed.	Yes	Yes

AGREE II = Appraisal of Guidelines for Research & Evaluation II; ASAM = American Society of Addiction Medicine; CCSMH = Canadian Coalition for Seniors' Mental Health.

Appendix 4: Main Study Findings and Authors' Conclusions

Summary of Findings From Included Systematic Reviews

de Andrade et al. (2019)⁸

Main Study Findings

Residential substance use treatment services for individuals with SUDs: Provide intensive care and support for individuals with severe and complex SUDs within an alcohol and drug-free, and 24-hour, residential community setting. Include alcohol and other drug withdrawal or maintenance management in a hospital or supervised residential facility, individual and group psychological support, mutual self-help and peer therapeutic communities, and support reintegration into community.

Quality assessment of the included studies by the authors:

- 23 studies (8 weak, 5 moderate, and 10 strong)

Treatment model comparison (8 studies; 4 strong, 2 moderate, 2 weak):

- RT versus pharmacotherapy versus detoxification (2 studies)
 - RT was associated with significant improvements in heroin abstinence, criminal activity, mental health, and physical health (Australian study, moderate quality).
 - RT had no significant impact on the number of offences committed (UK study, strong quality).
- Therapeutic community versus RT versus maintenance therapy (1 study)
 - No significant differences between groups in scores of mental health or quality of life (Iranian study, weak quality).
- RT versus outpatient (1 study)
 - Significantly higher proportion of patients receiving RT completed treatment (adjusted odds ratio [AOR] = 17.84; 95% confidence interval [CI], 8.91 to 35.73) and considered abstinence (AOR = 10.55; 95% CI, 5.84 to 19.06) compared to outpatients (South African study, weak quality).
- Inpatient withdrawal versus RT versus inpatient withdrawal + RT (1 study)
 - Combination of inpatient withdrawal and RT significantly increased the likelihood of no re-presentation to alcohol and other drug services within 6 months of index treatment completion (UK study, strong quality).
- RT with and without adjunctive therapy (3 studies)
 - RT + life enhancement treatment for substance use was associated with higher abstinence rates at 3 months, 6 months, and 12 months, and had significantly fewer adverse consequences at 12 months post-treatment compared with RT + supportive counselling (US study, strong quality).
 - RT + mindfulness-based relapse prevention was associated with significant reduction in substance use, craving, and stress compared with treatment as usual (RT + 12 step/self-help meeting) (US study, strong quality).

- Attending 2 or more sessions of mindfulness-based relapse prevention was associated with significant improvements in substance cravings and across a range of mental health outcomes (US study, moderate quality).

Substance use outcomes (17 studies; 7 strong, 5 moderate, 5 weak):

- 16 of 17 studies showed significant positive effects in substance use outcomes over time following RT. One study showed unclear results.

Mental health outcomes (17 studies; 7 strong, 5 moderate, 5 weak):

- 16 of 17 studies showed significant positive effect in mental health outcomes (psychological distress, post-traumatic stress disorder, depression, anxiety, stress, and general mental health) over time following RT. One study showed no significant difference in depression symptoms between RT groups with different adjunctive therapies.

Social outcomes (11 studies; 3 strong, 4 moderate, 4 weak):

- 0 of 11 studies reported a significant positive effect on social outcomes including quality of life, satisfaction, employment, and family and social relationships after RT treatment. One study showed unclear results.

Criminal activity (9 studies; 2 strong, 3 moderate, and 4 weak):

- 8 of 9 studies reported significant positive effect on criminal activity outcomes after RT treatment. One study showed significant reductions in recorded offences following inpatient detoxification and community-based pharmacotherapy programs but not RT.

Mortality (1 study; strong):

- Residential withdrawal (detoxification) services was associated with a high risk of death in the first year post-discharge.

Authors' Conclusion

Despite the growing need for effective residential substance use treatment internationally, the field continues to lack consensus-based guidelines. In line with previous reviews, this review on the most recent studies in the field (2013 – 2018) provide moderate quality evidence that residential treatment may be effective in reducing substance use and improving mental health. There is also some evidence that treatment may have a positive effect on social and offending outcomes. However, there remains a compelling need to conduct more research in this field that can address significant methodological flaws (particularly attrition) and test multicomponent service models. The challenges of conducting research in this setting may be partially overcome by the use of data linkage practices to monitor outcomes. With caution, current results point to a best practice approach to residential treatment that integrates mental health treatment, take a holistic approach to improving the overall health and wellbeing of the individual (beyond substance dependence), and provides continuity of care post-discharge. While there is some evidence of improved quality of studies in the field, there continues to be a strong need for investment in high quality research in residential drug treatment settings (particularly in developing countries) that translates to meaningful change in policy and practice.⁸ (p. 234).

Brooks et al. (2018)⁹

Main Study Findings

MAP: Administer regular doses of beverage alcohol or IV alcohol to people with AUD alongside related health and social supports.

Quality assessment of the included studies by the authors:

- 42 studies (no quality assessment provided)

Provision of alcohol to prevent or treat AWS in hospital settings (28 studies):

- 6 controlled studies compared MAP with other treatments or placebos for treating or preventing AWS. Alcohol was administered intravenously, orally, or both, and orally via nasogastric tube. Three studies found that MAP was effective in treating or preventing AWS, and 2 studies found that MAP was noninferior to the alternative treatments. One study was inconclusive.
- 2 uncontrolled studies used alcohol to treat AWS in trauma and burn patients, and found improvements in AWS. One uncontrolled study found variations in alcohol elimination rates in alcohol-dependent patients.
- 3 2-arm comparison studies concluded that alcohol is a safe and viable option to manage AWS in surgical patients (IV alcohol), trauma patients (IV alcohol), and hospitalized patients (beverage alcohol).
- 1 retrospective chart review found that patients had been inconsistently and inappropriately treated with alcohol, and only 10% were referred to addiction treatment. Another retrospective chart review found no significant difference in the Clinical Institute Withdrawal Assessment for Alcohol Scale scores between the alcohol group (beer or 50% distilled alcohol) and benzodiazepine group for the treatment of AWS.
- 4 case studies reported successful alcohol administration to treat AWS in hospital patients. One case study found no successful with alcohol treatment of AWS.
- 4 SRs provided mixed evidence. Two SRs published in 2013 reported the effectiveness of alcohol in preventing but not treating AWS. Two older SRs published in 1997 and 2004 found a lack of evidence to support the use of alcohol to treat or prevent AWS.
- 5 cross-sectional surveys of hospital administrators (4 in US and 1 in UK) found strong evidence that IV alcohol and beverage alcohol were prescribed to treat and prevent AWS.

MAP in community settings (14 studies):

- 1 pre- and post-analysis study of a shelter-based MAP in Toronto found that when participants were provided health and social supports and hourly doses of wine during daytime hours, the rates of incarcerations and time spent under community supervision were significantly reduced. Housing stability, hospitalizations, and detox admissions were improved.
- Another pre- and post-analysis of MAP in Ottawa, where participants received hourly doses of wine or sherry on demand from 7 a.m. to 10 p.m., reported a stabilized alcohol intake, decreased use of crisis services, improved personal hygiene, and compliance with medical care.
- 3 academic and 2 grey literature MAP case studies provided evidence that MAP could help clients to make changes in their alcohol consumption and reduce rates of hospitalization and crisis service utilization.

- 2 non-randomized controlled studies in Thunder Bay found that MAP was associated with a decreased consumption of alcohol, reduced rates of hospitalization and detox admission, and more positive interactions with police.
- Preliminary results of 2 grey literature articles, 1 in Thunder Bay and 1 in Vancouver, provided evidence that MAP was associated with improvements in housing stability and mental health measures, and reduction in alcohol consumption and alcohol-related harms.
- A non-peer-reviewed article from the Regional Municipality of Waterloo that reviewed MAP in 3 Canadian cities reported that MAP facilitated positive health and social outcomes.
- 1 Cochrane systematic review published in 2012 found no study that met its inclusion criteria in the assessment of the effectiveness of MAP in comparison with other interventions to reduce alcohol consumption.

Authors' Conclusion

Our review suggests that implementation of a hospital-based MAP is feasible and could potentially prevent uncomfortable alcohol withdrawal symptoms, stabilize patients' drinking patterns, discourage non-beverage alcohol consumption, encourage patients to stay in hospital and complete treatment, and connect them to other health and social supports. Future research is needed to develop and evaluate this harm reduction intervention in hospital settings, and identify its potential to reduce negative health outcomes amongst patients experiencing refractory AUDs and unstable housing.⁹ (p. S153)

Summary of Recommendations in Included Guidelines

ASAM, Lindsay et al. (2020)¹⁰

Recommendations

Summary of Recommendations

This guideline recommends expanding the concept of screening for alcohol use to further screen for the risk of experiencing withdrawal if consumption is stopped or decreased. These recommendations applied to all medical settings where patients at risk for alcohol withdrawal may be encountered.¹⁰ (p. 391)

This guideline also emphasizes the importance of evaluating a patient's risk of developing severe or complicated alcohol withdrawal or complications from alcohol withdrawal early in the assessment process.¹⁰ (p. 391)

This guideline also highlights the importance of level of care assessment, specifically, determining whether ambulatory or inpatient level of care is more appropriate. Although a few patient factors clearly identify inpatient settings as most appropriate, for the most part, placement decisions should involve careful considerations of a patient's individual risk factors for severe or complicated withdrawal or complications of withdrawal and the quality and availability of expertise and access to resources in the settings available.¹⁰ (p. 391)

In general, the guideline committee found that benzodiazepines remain the preferred medication for managing the signs and symptoms of alcohol withdrawal in most cases, particularly in preventing or treating severe withdrawal, seizures, or delirium.¹⁰ (p. 391)

This guideline also highlights that, to the fullest extent possible, patients undergoing alcohol withdrawal management should be engaged, if not initiated, in treatment for AUD as soon as cognitive status permit. This engagement should be considered part of the

withdrawal management process and should not be delayed until withdrawal management is complete.¹⁰ (p. 391)

Recommendations on Level of Care Determination

Recommendation III.1:

Level of care determination should be based on patient's current signs and symptoms, level of risk for developing severe or complicated withdrawal or complications of withdrawal, and other dimensions such as recovery capital and environment. Alcohol withdrawal can typically be safely managed in an ambulatory setting for those patients with limited or mitigated risk factors. Patients with low levels of psychosocial support or an unsafe environment may benefit from a more intensive level of care than is otherwise indicated.¹⁰ (p. 381)

Recommendation III.2:

*"Patients with active risk of suicide should be treated in a setting equipped to manage patients at risk of suicide, which often necessitates admission to an inpatient psychiatric setting that also provides withdrawal management services."*¹⁰ (p. 381)

Recommendation IV.5:

For patients managed in an ambulatory setting, the following indications would necessitate transfer to a more intensive level of care such as Level 2-WM (if in a Level 1-WM setting) or an inpatient setting:

- Agitation or severe tremor has not resolved despite having received multiple doses of medication, and the patient will not be continually monitored (eg, treatment setting is closing)
- More severe signs or symptoms develop such as persistent vomiting, marked agitation, hallucinations, confusion, or seizure
- Existing medical or psychiatric conditions worsen
- Patient seems over-sedated
- Patient returns to alcohol use
- Syncope, unstable vital signs (low/high blood pressure, low/high heart rate).¹⁰ (p. 383)

Quality of Evidence and Strength of Recommendations

None.

CCSMH, Bertram et al. (2020)¹¹

*"Accredited residential treatment should be considered as appropriate for treating CUD if the individual is unable to effectively reduce or cease their cannabis use."*¹¹ (p. 139)

Quality of Evidence and Strength of Recommendations

Level of evidence: Low

Strength of recommendation: Strong

Appendix 5: References of Potential Interest

Previous CADTH Reports

Inpatient and outpatient treatment programs for substance use disorder: a review of clinical effectiveness and guidelines. (*CADTH Rapid response report: summary with critical appraisal*). Ottawa (ON): CADTH; 2017: <https://cadth.ca/sites/default/files/pdf/htis/2017/RC0938%20In%20vs%20Outpatient%20Treatment%20for%20Substance%20Abuse%20Final.pdf>. Accessed 2021 May 26.

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