

# Canadian Clinical Guideline

## High Risk Drinking and Alcohol Use Disorder



**CRISM**



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Canada

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**Target Audience:**

Physicians, nurses and nurse practitioners, pharmacists, regulated health care professionals, and all other clinical and non-clinical personnel with and without specialized training in addiction medicine, who are involved in the care and management of individuals, families, and communities affected by alcohol use, high-risk drinking, and alcohol use disorder.

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## Territorial Acknowledgement

We would like to respectfully acknowledge that much of the development of this document occurred on the ancestral and unceded territory of the Coast Salish Peoples, including the traditional territories of the xʷməθkʷəyəm (Musqueam), Skwxwú7mesh (Squamish), and səliłwətał (Tseil-Waututh) Nations.

We recognize that the ongoing criminalization, institutionalization, and discrimination against people who use alcohol and other drugs disproportionately harm Indigenous peoples, and that continuous efforts are needed to dismantle colonial systems of oppression. We see our work connected to these efforts and hope that this guideline contributes to a system that provides safe, respectful evidence-based care.

## About the Canadian Research Initiative in Substance Misuse

Funded by the Canadian Institutes of Health Research (CIHR), the Canadian Research Initiative in Substance Misuse (CRISM) is a national research-practice-policy network focused on substance use disorders, comprising five interdisciplinary regional teams (Nodes) representing British Columbia, the Prairies, Ontario, Quebec, and the Atlantic region. Each CRISM node includes regional research scientists, service providers, policy makers, community leaders, and people with lived experience of substance use. CRISM's mission is to translate the best scientific evidence into clinical practice, health services, and policy change. More information about CRISM can be found at: <https://crism.ca>.

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## In Memoriam

Ron Kuhlke was a member of this committee and passed away in January 2021. Ron was an incredible advocate and champion for his community. He contributed to many initiatives including guidelines, education, and research projects through countless organizations. Ron was a well-known advocate in his single-room-occupancy building, where he successfully defended his neighbours against illegal eviction and played a critical role in forcing his landlord to restore the building's heat and hot water during a particularly cold winter. Ron's passing was an immense loss to the community and those who knew him and worked with him.

Randy Roberts was a committee member of this guideline and sadly passed away in January 2022. He was involved in several national organizations, including the Canadian Association of People who Use Drugs, and helped to create the Ontario Network of People Who Use Drugs (ONPUD) and the Brantford Substance Users Network. He was an outspoken advocate for the inclusion of people who use drugs in the decision and policy-making process, especially when the decisions would have a direct effect on their lives. He was grateful to be a part of this guideline and advocated for Indigenous peoples to have their own voices in this work. Randy is missed greatly and will be remembered for his contributions to his community and this guideline.

## Disclaimer for Health Care Providers

The recommendations in this guideline represent the view of the national guideline committee, arrived at after careful consideration of the available scientific evidence and following external expert peer review. The application of the recommendations in this guideline does not override the responsibility of health care professionals to make decisions that are appropriate to the needs, preferences, and values of an individual patient, in consultation with that patient and their family members or guardian(s), and, when appropriate, external experts (e.g., specialty consultation). When exercising clinical judgment in the treatment of high-risk drinking and alcohol use disorder, health care professionals are expected to take this guideline fully into account while upholding their duty to adhere to the fundamental principles and values of the Canadian Medical Association Code of Ethics, especially compassion, beneficence, non-maleficence, respect for persons, justice and accountability, as well as the required standards for good clinical practice defined by relevant governing bodies within regional or local jurisdictions. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

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The Guideline is intended to give an understanding of a clinical issue and outline one or more preferred approaches to the investigation and management of the issue based on best available evidence at the time of writing, while recognizing that the evidence base is continuously evolving. The Guideline is not intended as a substitute for the advice or professional judgment of a health care professional, nor is it intended to be the only approach to the management of a clinical issue. We cannot respond to patients or patient advocates requesting advice on issues related to medical conditions. If you need medical advice, please contact a health care professional.

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# Executive Summary

Despite the high prevalence of high-risk drinking, alcohol use disorder (AUD), and alcohol-related harms in Canada, these conditions frequently go unrecognized and untreated in the health care system. Research has shown that primary care providers can play an important role in the early detection and treatment of high-risk drinking and AUD and in connecting patients and families with specialized care services and recovery-oriented supports in their communities. However, the lack of an evidence-based guideline for the clinical management of high-risk drinking and AUD has resulted in low awareness and use of the full range of available treatment interventions among primary care providers in Canada.

To address this gap, a national guideline committee was convened to review the research evidence and reach consensus on recommendations for the clinical management of high-risk drinking and AUD. A set of 15 recommendations was derived by the committee, spanning the identification and clinical management of high-risk drinking and AUD in youth (aged 11–25 years) and adult patient populations, with a focus on primary care practice. The purpose of this guideline is to support health care providers with the implementation of evidence-based prevention, harm reduction, and treatment interventions for high-risk drinking and AUD in their scope of practice.

## Aims:

- Describe general principles of care for working with patients and families affected by alcohol use, high-risk drinking, and AUD
- Review strategies for alcohol use screening, diagnosis, and brief intervention for adult and youth patients who are drinking at high-risk levels
- Recommend strategies for ongoing AUD care, including use of psychosocial treatment interventions, pharmacotherapy, and community-based programs and supports
- Recommend a clinical algorithm for alcohol withdrawal management, where an individual's risk of developing severe complications is used to triage that individual to an appropriate care setting and management approach
- Provide guidance on outpatient withdrawal management

The guideline is intended to be a resource for physicians, nurses and nurse practitioners, pharmacists, regulated health care professionals, and all other clinical and non-clinical personnel with and without specialized training in addiction medicine who are involved in the care and management of individuals, families, and communities affected by alcohol use, high-risk drinking, and AUD. This guideline also serves as a resource for patients and their loved ones, to support treatment and wellness advocacy as well as promote systems-level quality improvement. In addition, this guideline is intended to be a resource for policy makers and health care administrators in the development of strategies and programs to best address unmet alcohol treatment and care needs within Canada in an evidence-based, cost-effective manner.



Table 1. Summary of Guideline Recommendations<sup>a</sup>

Recommendations
<i>(GRADE ratings for quality of evidence and strength of recommendation)</i>
<b>Screening, Diagnosis, and Brief Intervention</b>
<p><b>RECOMMENDATION 1:</b> When appropriate, clinicians should inquire about current knowledge of and offer education to adult and youth patients about Canada’s Guidance on Alcohol and Health, in order to facilitate conversations about alcohol use.</p> <p>(LOW, STRONG)</p>
<p><b>RECOMMENDATION 2:</b> All adult and youth patients should be screened routinely for alcohol use above low risk.</p> <p>(MODERATE, STRONG)</p>
<p><b>RECOMMENDATION 3:</b> All adult and youth patients who screen positive for high-risk alcohol use should undergo a diagnostic interview for AUD using the <i>Diagnostic and statistical manual of mental disorders, 5th ed, Text Revision (DSM-5-TR)</i> criteria and further assessment to inform a treatment plan if indicated.</p> <p>(LOW, STRONG)</p>
<p><b>RECOMMENDATION 4:</b> All patients who screen positive for high-risk alcohol use should be offered brief intervention.</p> <p>(MODERATE, STRONG)</p>
<b>Withdrawal Management</b>
<p><b>RECOMMENDATION 5:</b> Clinicians should use clinical parameters, such as past seizures or past delirium tremens, and the Prediction of Alcohol Withdrawal Severity Scale (PAWSS) to assess the risk of severe alcohol withdrawal complications and determine an appropriate withdrawal management pathway.</p> <p>(MODERATE, STRONG)</p>
<p><b>RECOMMENDATION 6:</b> For patients at low risk of severe complications of alcohol withdrawal (e.g., PAWSS &lt; 4), clinicians should consider offering non-benzodiazepine medications, such as gabapentin, carbamazepine, or clonidine for withdrawal management in an outpatient setting (e.g., primary care, virtual).</p> <p>(Gabapentin: MODERATE, STRONG; Carbamazepine, Clonidine: LOW, STRONG)</p>

a The GRADE approach<sup>1</sup> was used to assess the quality of evidence (possible categories include: high, moderate, low, or very low) and strength of recommendation (possible categories include: strong or conditional). Please refer to [Appendix 1: Methods](#) for more information on how the GRADE criteria were applied and an explanation of the quality of evidence and strength of recommendation scores.

**RECOMMENDATION 7:** For patients at high risk of severe complications of withdrawal (e.g., PAWSS  $\geq$  4), clinicians should offer a short-term benzodiazepine prescription ideally in an inpatient setting (i.e., withdrawal management facility or hospital). However, where barriers to inpatient admission exist, benzodiazepine medications can be offered in outpatient settings if patients can be closely monitored.

(HIGH, STRONG)

**RECOMMENDATION 8:** All patients who complete withdrawal management should be offered ongoing AUD care.

(LOW, STRONG)

## Ongoing Care—Psychosocial Treatment Interventions

**RECOMMENDATION 9:** Adults and youth with mild to severe AUD should be offered information about and referrals to specialist-led psychosocial treatment interventions in the community.

(MODERATE, STRONG)

## Ongoing Care—Pharmacotherapy

**RECOMMENDATION 10:** Adult patients with moderate to severe AUD should be offered naltrexone or acamprosate as a first-line pharmacotherapy to support achievement of patient-identified treatment goals.

A. Naltrexone is recommended for patients who have a treatment goal of either abstinence or a reduction in alcohol consumption.

B. Acamprosate is recommended for patients who have a treatment goal of abstinence.

(HIGH, STRONG)

**RECOMMENDATION 11:** Adult patients with moderate to severe AUD who do not benefit from, have contraindications to, or express a preference for an alternate to first-line medications can be offered topiramate or gabapentin.

(Topiramate: MODERATE, STRONG; Gabapentin: LOW, CONDITIONAL)

**RECOMMENDATION 12:** Adult and youth patients should not be prescribed antipsychotics or SSRI antidepressants for the treatment of AUD.

(MODERATE, STRONG)

**RECOMMENDATION 13:** Prescribing SSRI antidepressants is not recommended for adult and youth patients with AUD and a concurrent anxiety or depressive disorder.

(MODERATE, STRONG)

**RECOMMENDATION 14:** Benzodiazepines should not be prescribed as ongoing treatment for AUD.

(HIGH, STRONG)

## Community-based Supports and Programs

**RECOMMENDATION 15:** Adults and youth with mild to severe AUD should be offered information about and referrals to peer-support groups and other recovery-oriented services in the community.

(MODERATE, STRONG)

# 1 Introduction to the Guideline

This introduction describes the background, rationale, overall structure, scope, and intended use of the guideline.

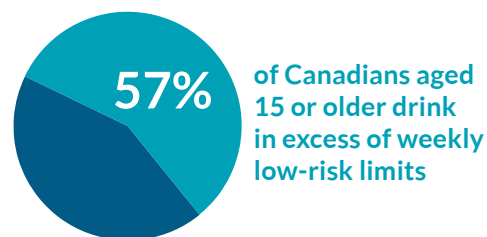
## 1.1 Background and Rationale

In 2019, three-quarters (76% or 23.7 million) of people living in Canada reported consuming alcohol in the past year.<sup>2</sup> The reasons that people use alcohol vary from celebration and relaxation to coping with pain or trauma. Like other substance use, alcohol use occurs on a spectrum, and the health and social effects can range from non-harmful to harmful. The social and structural context (e.g., social norms, colonization, racism, classism, homophobia, transphobia) impacts individual alcohol use, patient–provider relationships, and ultimately, the health outcomes of patients.

High-risk drinking and alcohol use disorder (AUD) can have significant health, social, and economic consequences for individuals and communities. Alcohol use disorder is a potentially chronic, relapsing medical condition characterized by clinically significant impairment or distress from the use of alcohol.<sup>3</sup> Individuals with AUD may continue to consume alcohol despite adverse social, occupational, legal, or health effects.<sup>4</sup> Individuals who drink before the age of 15 are significantly more likely to develop AUD, and earlier age at first use is associated with a higher prevalence of alcohol-related harms later in life.<sup>5-7</sup>

**This guideline defines high-risk drinking based on the score from the Alcohol Use Disorders Identification Test (AUDIT) or its condensed version (AUDIT-C). High-risk drinking is defined by an AUDIT score of 16 or higher or an AUDIT-C score of 8 or higher. See [Appendix 2](#) for details. Note that other screening tools and *Canada's Guidance on Alcohol and Health* have independent definitions of high-risk drinking.**

Alcohol use disorders and high-risk drinking are common in Canada.<sup>8</sup> It is estimated that 57% of Canadians aged 15 or older currently drink in excess of weekly limits recommended by *Canada's Guidance on Alcohol and Health* (more than 2 drinks per week)<sup>8</sup> and in 2012, 18% of all Canadians aged 15 or older had met the clinical criteria for an AUD during their lifetime.<sup>9</sup> Data from the World Health Organization's 2021 World Health Statistics report shows that per capita alcohol consumption for individuals aged 15 and older in Canada is 52% higher than the global average and among the highest for developed countries.<sup>10</sup> Among youth, the 2018–2019 Canadian Student Tobacco, Alcohol and Drugs Survey demonstrated that almost a quarter of students in grades 7 to 12 reported binge drinking (5 or more drinks on one occasion) within the past year.<sup>11</sup>



**4.1%**  
of all deaths  
in Canada are  
attributable  
to alcohol use

Nearly 200 disease or injury conditions can be wholly or partly attributable to alcohol use, including cancer, cardiovascular disease, liver disease, lower respiratory infections, and injuries from violence or motor vehicle accidents.<sup>12,13</sup> National statistics indicate that in 2016, alcohol use caused 10,500 deaths (4.1% of all deaths) and 6.3% of all potential years of life lost for individuals aged 15 and older in Canada, with higher proportions in younger age groups.<sup>14</sup> Globally, alcohol was responsible for an estimated 3 million deaths (5.3% of all deaths) in the same year<sup>12,14</sup> and, for the population aged 15–49 years, was the leading risk factor for premature death and disability.<sup>15</sup>

Economic, health care, legal, and social costs associated with alcohol use are substantial. In 2017, the overall annual economic cost of substance use in Canada was estimated to be \$46 billion.<sup>16</sup> Alcohol use was associated with the greatest proportion of these costs (lost productivity, health care,

**\$16.6 billion:**  
Total economic cost of alcohol  
use in Canada in 2017

criminal justice, other direct costs), accounting for about \$16.6 billion or 36% of the total, followed by tobacco (\$12.3 billion; 27%), and all other substances<sup>b</sup> (\$17.1 billion; 37%).<sup>16</sup> Alcohol consumption can decrease inhibitions and increase behaviours that can lead to a variety of negative outcomes, for example, interpersonal conflict and financial problems, workplace accidents, traffic accidents, and deaths.<sup>17</sup> Alcohol is often associated with incidents of violence committed by intimate partners and unknown perpetrators, as well as theft and property crime.<sup>16,18-20</sup>

In the 2019–2020 fiscal year, the rate of hospitalizations wholly attributable to alcohol in Canada was 258 per 100,000 people aged 10 and older, exceeding the rate of hospitalizations due to heart attacks (241 per 100,000 people aged 10 and older). Hospitalizations wholly attributable to alcohol were 4 times more common than those caused by opioids (alcohol: 240 hospitalizations per day; opioids: 55 hospitalizations per day). Provincial estimates for hospitalizations wholly attributable to alcohol ranged from 159 to 1,759 per 100,000 people aged 10 and older (in New Brunswick and Northwest Territories, respectively).<sup>21</sup> The average cost per hospitalization wholly attributable to alcohol in Canada was estimated to be \$8,100 (compared to \$5,800 for the average hospital stay), largely a result of the longer length of stay for alcohol-caused hospitalizations compared to the average hospitalization (11 versus 7 days).<sup>22</sup>

Despite the significant burden of disease, social harms, and economic costs attributed to alcohol in Canada, high-risk drinking and AUD frequently go unrecognized and untreated in the health care system.<sup>23,24</sup> Recent research has highlighted the important role that primary care providers can have in early detection and intervention for high-risk drinking; outpatient withdrawal management; treatment of AUD; and connecting patients and families with specialized services and community-based supports.<sup>25</sup> Although high-risk drinking and AUD can be readily identified using simple screening tools, alcohol use screening is not widely implemented in primary care practice.<sup>26</sup> This is a critical missed opportunity to intervene early when many individuals, including

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b The “other substances” category included cannabis, opioids, other central nervous system (CNS) depressants (e.g., benzodiazepines, barbiturates), cocaine, other CNS stimulants (e.g., amphetamine, methamphetamine, ecstasy) and other substances (e.g., hallucinogens, inhalants) as per the original source.<sup>16</sup>

adolescents and young adults, may respond positively to brief counselling interventions alone and change their behaviour to reduce their risk of alcohol-related harms.<sup>26</sup> These opportunities for early intervention, treatment, and support are missed if providers rely on AUD case identification alone.

Screening also serves an important role in identifying individuals with moderate to severe AUD who would benefit from more intensive approaches, including pharmacotherapy, psychosocial treatment interventions, and community-based recovery and wellness-oriented services. Despite evidence of benefit, individuals with AUD rarely receive evidence-based treatment interventions.<sup>27,28</sup> Although Canadian statistics are lacking, in the United States, national surveys indicate that fewer than 8% of individuals with AUD had received treatment in the past 12 months.<sup>29</sup> European countries report similarly low rates, with less than 20% of people with AUD receiving any kind of treatment.<sup>30</sup>

For patients with moderate to severe AUD who identify cessation or reduction of alcohol use as a treatment goal, there is a range of psychosocial and pharmacological treatments available across Canada. Emerging research shows that treatment and lowering alcohol consumption do result in meaningful reductions in morbidity and mortality for people with AUD.<sup>31,32</sup> Despite this effectiveness, the two first-line medications currently approved in Canada, naltrexone and acamprosate, appear to be critically underutilized.<sup>28</sup> Data are sparse; however, a study in Ontario found that over a one-year period, only 37 of 10,394 (0.4%) public drug plan beneficiaries diagnosed with AUD filled a prescription for naltrexone or acamprosate in the year following their diagnosis.<sup>33</sup> Similarly, a 2021 report from Manitoba found that only 493 of 37,388 individuals (1.3%) diagnosed with AUD had a prescription dispensed for naltrexone, acamprosate, or disulfiram within the 20-year study period.<sup>34</sup> Conversely, patients with concurrent AUD and mental health conditions (e.g., depression, anxiety) are frequently prescribed psychotropic medications (e.g., antidepressants, antipsychotics) which have not been effective in reducing drinking or improving mood in this population.<sup>35,36</sup> Likewise, effective psychosocial interventions are underutilized. Though comparable data are not available in Canada, the United States Department of Veteran Affairs found that only 5.5% of patients drinking above low risk received brief intervention.<sup>37</sup>

The cumulative result of failure to provide evidence-based care for AUD is a system where patients and providers alike remain focused on attempting to address the negative consequences of alcohol use (e.g., hypertension, liver disease, depression) rather than effectively preventing or reducing harm through early intervention and AUD-specific treatment. Patients have expressed barriers to seeking care, including internal barriers (e.g., belief that they should be strong enough to handle it alone or that the problem would get better by itself) and stigma,<sup>38</sup> and a lack of information about pharmacotherapy<sup>39</sup> and other treatment options. Provider-level barriers to the use of pharmacotherapy for substance use disorders include inadequate training, a lack of information about pharmaceutical treatments, and misperceptions about effectiveness of medications.<sup>39</sup> Logistical issues such as lack of access to physicians and limited clinical and administrative support may further constrain provision of treatment.<sup>39</sup>

These trends underscore the importance of bridging the gap between research and clinical practice, particularly in primary care, to generate meaningful improvements in health and well-being for individuals, families, and communities impacted by alcohol use.

### **Canada is in urgent need of a paradigm shift in the clinical management of AUD.**

To move this agenda forward, this committee sought to address the lack of evidence-based practice recommendations available to health care providers. A panel of Canadian experts was convened to review the literature and develop an evidence-based guideline for the optimal screening, diagnosis, treatment, and care of individuals with AUD. It is anticipated that health care professionals, policy makers, and educators will use this document to inform clinical practice and health promotion activities directed toward reducing alcohol-related harms within the country.

## 1.2 Scope and Purpose of the Guideline

This guideline provides information and guidance on the identification and clinical management of high-risk drinking and AUD in adults (individuals aged 26 years and older) and youth (individuals aged 11–25 years). This guideline is meant to support routine screening to identify high-risk alcohol use and diagnose AUD, and to promote the use of evidence-based treatment, wellness and recovery-oriented interventions, and risk and harm reduction within primary care and other clinical or community-based settings in Canada. This guideline acknowledges the wide variability in access to specialist services including inpatient withdrawal management, consultative services, and other specialized AUD services across the country may limit application of some of the recommendations.

### 1.2.i Intended Audience

The guideline is intended to be a resource for physicians, nurses and nurse practitioners, pharmacists, regulated health care professionals, and all other clinical and non-clinical personnel with and without specialized training in addiction medicine who are involved in the care and management of individuals, families, and communities affected by alcohol use, high-risk drinking, and AUD. This guideline also serves as a resource for patients and their loved ones, to support treatment and wellness advocacy as well as promote systems-level quality improvement. In addition, this guideline is intended to be a resource for policy makers and health care administrators in the development of strategies and programs to best address unmet alcohol treatment and care needs within Canada in an evidence-based, cost-effective manner.

### 1.2.ii Care Settings

While this guideline focuses on the clinical management of AUD in primary care settings (e.g., family practice clinics, community health centres, walk-in clinics, student health services), the recommendations also apply more broadly to other care settings and environments that may represent an individual's first contact with the health care system (e.g., emergency departments, other acute care



settings, sexual health services, prenatal care clinics, and specialized mental health and addiction services). Clinical care teams and staff in these health care settings are encouraged to adapt and apply guideline recommendations as needed for their practice to support individuals and families affected by alcohol use, high-risk drinking, and AUD in seeking help and accessing evidence-based treatment and services at multiple points of entry in the health care system.<sup>40</sup>

### 1.2.iii Patient Populations

The recommendations made in this guideline are applicable to the general adult patient population, which can include individuals who are drinking within recommended limits for low-risk drinking, those whose alcohol use exceeds low-risk alcohol drinking limits, individuals diagnosed with AUD of any severity (mild, moderate, or severe),<sup>3</sup> and individuals in recovery from AUD. While much of the evidence reviewed in this guideline was obtained from studies of individuals in the general adult population, it is the consensus of the guideline committee that guideline recommendations may be relevant and applicable to youth, after thorough consideration of risks and benefits. This guideline defines adolescents as individuals aged 11–17 years, young adults as individuals aged 18–25 years, and youth as individuals aged 11–25 years (i.e., inclusive of adolescent and young adult age categories). Although there is a lack of AUD research specific to youth, particularly in adolescents, this guideline includes abbreviated evidence-based guidance for screening, diagnosis, brief intervention, withdrawal management, and AUD pharmacotherapy in youth, based on evidence where available and committee consensus.

Additionally, while this guideline offers a brief overview of the available evidence for the clinical management of high-risk drinking and AUD in pregnant individuals,<sup>c</sup> the importance of specialist consultation in these cases is

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- c While the majority of pregnant people identify as women, this term does not reflect the identities and experiences of all pregnant people, some of whom do not identify as female or as women. This guideline has adopted the practice of using gender-neutral language in pregnancy-related guidance to support inclusivity of sex- and gender-diverse patient populations. Asking patients how they choose to identify themselves and using their correct pronouns (e.g., they/them/theirs, she/her/hers, he/him/his) is an important component of person-centred care.

emphasized, as is the urgent need for more research in this area. For additional clinical guidance on the management of alcohol use during pregnancy and postpartum, clinicians can refer to [Screening and Counselling for Alcohol Consumption During Pregnancy](#)<sup>41</sup> issued by the Society of Obstetricians and Gynaecologists of Canada. Additional resources can be found at [helpwithdrinking.ca](http://helpwithdrinking.ca).

It should be noted that, like other topics, the vast majority of AUD research has been conducted with white adult men; individuals inhabiting other marginalized identities (e.g., due to gender, race) have historically been excluded from most research. Specific populations and communities, including Indigenous peoples, women, 2S/LGBTQ+<sup>d</sup> individuals, pregnant people, youth, older adults (age 65 and over), individuals with concurrent mental health disorders, individuals experiencing homelessness, and rural and remote populations may have unique health needs and circumstances due to biological or societal factors. A brief overview of additional considerations for providing care to these populations, including links to resources, has been included in [Working with Specific Populations](#).

#### **1.2.iv Addressing a Need for Evidence-Based Medicine in AUD Care**

Evidence-based medicine is an approach to patient care that is guided by the best available evidence from clinical research. While evidence-based medicine principles have been increasingly accepted in other areas of medicine, practices for AUD treatment have been slow to adopt more evidence-informed approaches.<sup>42,43</sup> This is due to structural issues (e.g., lack of training of health

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- d The acronym 2S/LGBTQ+ has been used in this guideline to describe Two-Spirit, lesbian, gay, bisexual, transgender, queer, and other gender and sexually diverse individuals. This guideline has adopted the practice of placing “2S” for “Two-Spirit” at the beginning of this acronym to acknowledge Indigenous ways of knowing gender and sexuality and the long history of gender and sexual diversity in Indigenous cultures. It is important to note that not all Indigenous LGBTQ+ people identify as Two-Spirit, and that not all Indigenous cultures perceive Two-Spirit identities in the same way. Asking patients how they prefer to identify themselves rather than assuming their gender identity or sexuality is an important component of person-centred care.

care providers in addiction medicine, stigma),<sup>43,44</sup> and the lack of evidence-based guidelines has also been noted as a barrier.

In this regard, the current state of care for persons with alcohol-related challenges is particularly alarming. Despite the substantial amount of research available to guide AUD care, interventions with proven effectiveness are rarely offered to individuals with AUD.<sup>42,45</sup> In the absence of evidence-based guidelines and poor access to experienced providers and services, individuals with AUD who seek care often receive ineffective and potentially harmful interventions.<sup>46-50</sup> Due to the under-treatment of AUD, hospitalizations for alcohol-related harms in Canada outnumber the rate of hospitalizations for heart attacks.<sup>21</sup>

When new guidelines present novel recommendations, care providers may be presented with evidence that challenges the effectiveness of interventions they previously thought to be helpful. In this context, the primary focus of previous AUD guidelines has been to promote effective interventions; considerably less attention has been directed toward identifying and discouraging interventions that may be less effective or even harmful.<sup>51</sup> This guideline examined both effective and ineffective strategies guided by systematic literature searches and evidence-based medicine principles whereby meta-analyses of randomized controlled trials, where available, were given the most weight in developing the recommendations. Accordingly, while further research to improve AUD care in specific populations is urgently needed, advancing the utilization of evidence-based practices—as articulated in this guideline—has the potential to dramatically reduce morbidity and mortality from alcohol-related harms in Canada.

## 1.3 Methods

Description of the methods used to conduct the structured review of the literature, develop recommendations for clinical practice, and assess quality of evidence and strength for each recommendation can be found in [Appendix 1: Methods](#).

# 2 Principles of Care

The committee identified several overarching principles of care that apply to all recommendations and clinical care guidance offered in this guideline and, more broadly, to establishing positive partnerships with patients and families experiencing alcohol-related harms. These principles include the importance of considering the social determinants of health and incorporating harm reduction, trauma- and violence-informed practice, and culturally safe approaches as the standard of care for patients and families affected by alcohol use, high-risk drinking, and AUD. The committee endorses an integrated and comprehensive medical management strategy and the use of patient-centred, recovery- and self-defined wellness oriented, and family-oriented approaches to optimize health, wellness, and social outcomes of patients and families.

The principles of care are intended to serve as a general framework to support clinicians, care teams, and programs in the integration of care for high-risk drinking and AUD in their clinical practice. Clinicians and care teams are encouraged to review and adapt these principles of care as needed to fit their local context and resources available. These principles of care should not be considered an exhaustive list; there may be additional factors clinicians should consider in different practice settings or when working with specific patients, families, communities, and populations (see [Working with Specific Populations](#)).

## Principles of Care

<b>Social Determinants of Health</b>	<b>Patient-Centred Care</b>	<b>Trauma- and Violence-Informed Practice</b>	<b>Anti-Racist Practices</b>	<b>Indigenous Cultural Safety and Humility</b>
<b>Harm Reduction</b>	<b>Recovery and Wellness-Oriented Care</b>	<b>Integrated Continuum of Care</b>	<b>Comprehensive Health Management</b>	<b>Family and Social Circle Involvement</b>

## 2.1 Social Determinants of Health

The social determinants of health can be understood as “the broad range of personal, social, economic, and environmental factors that determine individual and population health.”<sup>52</sup> At a population level, this can be understood as the quantity and quality of resources a society makes available to all of its members, which include, but are not limited to: childhood conditions; access to income; education and literacy; food, housing, and employment; working conditions; and health and social services.<sup>52,53</sup> Distribution of these resources tends to occur along a social gradient,<sup>54</sup> and is shaped by factors such as socioeconomic class and income; sex, gender identity, and sexuality; Indigeneity; race and ethnicity; citizenship status; and disability status.<sup>53,55</sup> These factors are often interrelated and intersectional—meaning that people occupy multiple social positions by nature of their unique identity and that these factors interact with and impact each other.<sup>56</sup> People who belong to marginalized groups or occupy the lowest socioeconomic classes experience the most significant barriers to accessing resources and, in turn, have the poorest health outcomes.<sup>55</sup>

Alcohol use, high-risk drinking, and AUD should also be viewed within this larger social context. Higher prevalence rates of high-risk drinking and AUD are observed among individuals who report adverse early childhood experiences,<sup>57</sup> lower socioeconomic status,<sup>58</sup> living in poorer neighbourhoods,<sup>59</sup> and who experienced discrimination due to race, ethnicity, sexuality, or gender.<sup>60</sup>

Clinicians, care teams, and staff should have an understanding of how the unequal distribution of power, opportunity, and resources in Canadian society impacts the social determinants of health for individuals.<sup>55</sup> Clinicians providing care to individuals, groups, and communities at risk of discrimination and marginalization beyond that related to alcohol and other substance use should endeavour to remove barriers to accessing care that such patients may experience. The Canadian Institutes for Health Research (CIHR)-funded EQUIP Health Care provides several resources as well as the [EQUIP Equity Action Kit](#) to support organizations to implement equity-oriented care. Additionally, clinicians should aim to address inequities that may exist related to the social determinants of health by connecting patients with resources to meet their social and survival needs (e.g., housing, food/nutrition, financial assistance, employment).

## 2.2 Patient-Centred Care

Patient-centred care is about meaningful partnership between the patient and provider. It considers the unique needs, values, and preferences of each patient. It aims to engage and empower patients as experts in their own care, including acting as the primary agent for reducing harms related to substance use, setting individualized treatment goals that are realistic and meaningful, and collaboratively selecting treatment options or interventions that will best support achieving their individual goals.<sup>61,62</sup> Patient-centred care encompasses a variety of approaches that attempt to account for power imbalances and experiences of marginalization.

Research suggests that incorporating patient-centred approaches in the clinical management of AUD can improve retention in care, treatment satisfaction, and health outcomes.<sup>63</sup> Practical strategies for incorporating patient-centred care in the clinical management of AUD include<sup>61</sup>:

- Collaboratively developing treatment plans
- Encouraging patients to set treatment goals that are meaningful to them (and not imposing goals on them)
- Using a shared decision-making framework to select treatment options or interventions
- Being open to and respectful of patient agency and choice

Clinicians, care teams, and staff should be aware of and actively work to reduce the stigma experienced by individuals with AUD, including awareness of the language they use in clinical encounters and its potential to stigmatize individuals who use alcohol and other substances. Clinicians and staff involved in substance use care should strive, at all times, to use “person-first” language and current medical terminology (e.g., person with alcohol use disorder) when interacting with patients, families, colleagues, health care professionals, and staff.<sup>64</sup>

While patients may choose to refer to themselves and their health conditions using language that they are most comfortable with, clinicians, other health

care professionals, and non-clinical staff should also avoid using non-diagnostic, stigmatizing, or slang terms (e.g., “alcoholic”, “addict”, “[alcohol] abuse”) in conversation and when charting. Use of such terms by health care providers has been shown to be stigmatizing to some patients<sup>65,66</sup> and to influence the behaviors of subsequent clinicians when included in a medical record.<sup>67</sup> Stigma—both experienced and anticipated—has been associated with a reduced likelihood of accessing and staying in care<sup>68-70</sup> as well as receiving lower quality care.<sup>67</sup> Clinicians are encouraged to review [Communicating About Substance Use in Compassionate, Safe and Non-Stigmatizing Ways](#),<sup>71</sup> a resource developed by the Public Health Agency of Canada, for more information.

## 2.2.i Clinical Flexibility in Response to Local or Global Events and Reducing Barriers

Patient-centred care includes providing access to services and treatments without undue barriers. Care teams should strive to assess a patient’s needs and ability to access treatment and facilitate low-barrier solutions. Events over recent years, including the COVID-19 pandemic and climate emergency-related phenomena (e.g., wildfire evacuations, weather warnings due to extreme heat, flooding) have demonstrated the necessity and feasibility of clinical flexibility that prioritizes patient safety and continuity of care. Patient care should be adapted, as needed, during local or global emergencies and disruptions, to ensure that patients can continue to access life-saving treatment without putting their health at risk or facing unreasonable barriers. Examples of adaptations may include shifting toward virtual care, facilitating transfer of prescriptions to a new pharmacy, or engaging other health care providers to support the care plan, including medication management. Prescribers are encouraged to access local/provincial specialist consultation if needing support to adapt care plans in response to states of emergency or other disruptive events. Exceptions to standard clinical care should be documented, including the rationale, patient discussion, and patient consent.

## 2.3 Trauma- and Violence-Informed Practice

Research has shown that individuals with AUD are more likely to have experienced past trauma or have a diagnosis of post-traumatic stress disorder (PTSD) compared to the general population.<sup>29,72,73</sup> Accordingly, this guideline strongly recommends that clinicians and care teams be familiar with and follow the principles of trauma- and violence-informed practice when working with patients and families affected by alcohol, high-risk drinking, and AUD.

The goal of trauma- and violence-informed practice is to create a safe and respectful environment that minimizes the potential for harm and re-traumatization of patients.<sup>74</sup> Consistent and universal adherence to trauma- and violence-informed approaches in all aspects of clinical practice help create a supportive setting for all patients and families, whether or not they have experienced trauma or violence in their lives.<sup>75</sup> The key principles of trauma- and violence-informed practice are trauma awareness; safety and trustworthiness; choice, collaboration, and connection; and strengths-based approaches and skill building.<sup>74</sup>

While a universal approach to trauma- and violence-informed practice is recommended, it is recognized that some patient populations are more likely to have experienced trauma and violence than others. For example, Indigenous peoples, women, and 2S/LGBTQ+ populations are more likely to have experienced trauma and violence as a result of racism, discrimination, and social inequity compared to other patient populations.<sup>76,77</sup>

It is important to note that disclosure of violence and trauma is not the goal of trauma and violence-informed practice; health care providers do not necessarily need to know an individual's past experiences to provide appropriate support. Additionally, trauma- and violence-informed care is not intended to treat trauma. Clinicians should be familiar with crisis services and specialized treatment and support services in their community for individuals who have experienced trauma, and provide information and referrals to patients, should the need arise.



## Trauma- and violence-informed care resources

The BC Centre of Excellence in Women's Health's [New Terrain](#) toolkit<sup>78</sup>

[The VEGA \(Violence, Evidence, Guidance, and Action\) Project](#) has pan-Canadian, evidence-based guidance and education resources for recognizing and responding to family violence

The Manitoba Trauma Information and Education Centre's [The Trauma-Informed Toolkit](#)<sup>79</sup>

The Substance Abuse and Mental Health Services Administration's (SAMHSA) [Trauma-Informed Care in Behavioral Health Services](#)<sup>80</sup>

EQUIP Health Care's [Trauma- and Violence-Informed Care Tool](#)<sup>81</sup> for organizations and care providers, and self-directed [Trauma- and Violence-Informed Care Workshop](#) and [Trauma- and Violence-Informed Care Curriculum](#) with practical guidance on how to provide care in a trauma- and violence-informed way

[Decolonizing Trauma Work: Indigenous Stories and Strategies](#) by Renee Linklater explores healing and wellness in Indigenous communities on Turtle Island.

## 2.4 Anti-Racist Practices

Racial/ethnic discrimination has been significantly associated with a higher risk of negative alcohol-related outcomes among communities of colour.<sup>82-85</sup> For example, a 2016 systematic review (N = 97, predominantly focused on African American participants) found that racial discrimination was associated with a higher risk of heavy alcohol use and AUD.<sup>85</sup> Additionally, a 2020 US national survey analysis (n = 17,115) examining the correlation between racial discrimination and AUD severity found that, in comparison to those who did not experience discrimination, individuals who experienced discrimination had a 1.5-fold greater risk of mild AUD, a 1.6-fold greater risk of moderate AUD, and a 2.3-fold greater risk of severe AUD based on the DSM-5-TR criteria.<sup>84</sup> Referring to literature that identifies discrimination as a stressor, the authors hypothesize that the participants used alcohol to cope with the effects of interpersonal and systemic racism.<sup>84,85</sup> Research has also shown that members of racialized communities face more barriers to treatment access, lower retention, and reduced satisfaction compared to their white counterparts, due to the experience of discrimination within the health care system.<sup>82,83</sup>

The implementation of an anti-racist framework for substance use care can help improve care engagement and health outcomes for racialized clients and

other populations that experience marginalization.<sup>86</sup> By definition, anti-racism is a process of confronting and interrogating racist structures that persist within current sociocultural institutions, including the health care system.<sup>86,87</sup> Anti-racist practices require individuals to build awareness of their own position and role within these systems and actively challenge norms, policies, and practices that marginalize racialized members of society.<sup>86,87</sup>

**Examples of inclusive, anti-racist policies and program development considerations include<sup>88-90</sup>:**

- Seek pre-implementation consultation from members of racialized and ethnically<sup>e</sup> diverse communities that the program serves
- Prioritize racial and ethnic diversity and equity in employee hiring and retention practices
- Anti-racism training for all staff
- Build partnerships with community organizations that support members of racialized communities
- Tailor treatment plans and approaches to specific cultural/racial groups

**Examples of service elements that can support members of racialized communities may include<sup>88,91</sup>:**

- Provide interpretation and translation services to clients for whom language is a barrier to equitable program participation
- Ensure that client materials are provided in the client's language, and at an appropriately accessible reading level
- Include a strong outreach component, as people who are new to Canada, or to a given province or territory, may be unaware of the types of substance use

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e Race refers to a social construct used to categorize groups of people based on physical characteristics such as skin tone, hair texture, and facial features. Ethnicity refers to a group of people who share broader cultural experiences such as language, customs, food, nation, and religion.

- support services available or how to access them
- Provide space and other necessities for religious or cultural practices
  - Establish a confidential, clearly-defined, and communicated procedure for clients and employees to safely report racial discrimination

## 2.5 Indigenous Cultural Safety and Humility

Abundant evidence has demonstrated that historic and present-day colonialism has disrupted the health and well-being of Indigenous peoples in what is colonially known as Canada. Decades of federal policies with the sole purpose of eradicating Indigenous identities, families, communities, culture, and traditional ways of life (i.e., genocide) have resulted in multigenerational trauma, racism, and discrimination.<sup>92-94</sup> These factors manifest as an overall increased risk of premature morbidity and mortality among Indigenous peoples in Canada relative to non-Indigenous people in Canada.<sup>95-97</sup> Epidemiological data that show higher prevalence rates of high-risk substance use, substance use disorders, and substance-related harms among Indigenous peoples<sup>95,98</sup> must be interpreted within this broader context. More specifically, it is emphasized that Indigenous peoples are not, by nature of their genetic background or cultural identity, a “high-risk” population; rather, the settler state’s approach of erasure, displacement, and assimilation of Indigenous peoples has led to significant health and social inequities and created conditions where some individuals use alcohol and other substances to cope.<sup>69,70</sup> Racism and stigma about Indigenous peoples, particularly around alcohol and other substance use,<sup>71-73</sup> persists within Canadian society and the health care system, which deters this population from seeking out and staying engaged in care.<sup>74-76</sup>

If the mainstream Canadian health care system is to be effective in addressing health and social inequities experienced by Indigenous peoples, health care providers must make a meaningful commitment to providing culturally safe and culturally appropriate care.<sup>99</sup> Indigenous cultural safety is an approach that

moves beyond the concept of cultural sensitivity<sup>f</sup> to consider how social and historical contexts, institutional discrimination, structural and interpersonal power imbalances, and past, current, and ongoing colonization shape health and health care experiences of Indigenous peoples. Cultural safety is defined by those receiving the care, not those delivering the care.<sup>101</sup> It requires health care providers to be knowledgeable about past and present day colonialism and the roots of historical, ongoing, and multigenerational trauma among Indigenous peoples, and to practice cultural humility: to be continually self-reflective of personal biases and aware of their position of power and the effects that this power dynamic may have on Indigenous peoples in health care settings.<sup>100</sup>

**Specific approaches and understandings have been identified as necessary to provide culturally safe and appropriate care to Indigenous peoples,<sup>100,102</sup> which include:**

- Understanding the importance of local history and the lasting and multigenerational impacts of colonization and the residential school system
- Examining, understanding, and acknowledging how health care providers' own values, including potentially moralistic views on alcohol and other substance use, impact the health care environment and health care encounters
- Understanding how power imbalances due to differences in education, social status, and class impact encounters with health care providers
- Understanding health as encompassing physical, mental, emotional, and spiritual well-being
- Understanding the impacts of disparities in the social determinants of health
- Respecting local Indigenous knowledge, traditions, traditional beliefs, and healing practices

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<sup>f</sup> Cultural sensitivity respects cultural differences and involves communicating and behaving in ways that are considered polite and respectful by the person of the other culture.<sup>100</sup>

- Recognizing and respecting differences in communication styles, which may be influenced by power imbalances as well as culturally-specific behaviours<sup>g</sup>
- Understanding that whole communities may be impacted by what happens to one community member, that the family unit may be a large, extended family, and that hostile health care experiences can influence entire communities' health care seeking attitudes
- Understanding that cultural healing practices may require that families be involved in the care of clients
- Approaching patient relationships with respectful curiosity
- Challenging personal assumptions, being flexible, and being open to changing how things are commonly done
- Recognizing and accommodating the need for a translator for those whose primary language is not English

**As a starting point, this document strongly recommends that all health care professionals and staff undertake Indigenous cultural safety training.**

To improve their ability to establish safe, positive partnerships with Indigenous clients and families, care teams and staff are also encouraged to familiarize themselves with the [Truth and Reconciliation Commission Reports](#), specifically the [Calls to Action](#), which outline necessary actions to address the legacy of colonialism in a range of domains including health care.

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<sup>g</sup> For example, less eye contact, long silences, and not answering direct questions or replying with a story or longer narrative response may be the norm for some Indigenous peoples compared to non-Indigenous populations.

## Indigenous cultural safety training programs

The [National Indigenous Cultural Safety Collaborative Learning Series](#)

The [Ontario Indigenous Cultural Safety Program](#)

Nunavut Program's [Cultural Competency Modules](#)

The [Saskatoon Health Region Cultural Competency & Cultural Safety Tool Kit](#)

The [Manitoba Indigenous Cultural Safety Training](#)

The [San'yas Indigenous Cultural Safety Training Program](#) offered by the Provincial Health Services Authority (PHSA) Aboriginal Health Program in BC

First Nations Health Authority (FNHA) and BC Client Safety & Quality Council's [Cultural Safety and Cultural Humility Webinar Action Series](#)

[Reconciliation Education](#) online course

An online course titled [New Respect Indigenous Cultural Safety](#) presented by Public Health Training for Equitable Systems Change (PHESC)

A comprehensive 12-module free online course titled [Indigenous Canada](#) offered by the University of Alberta Faculty of Native Studies, which is designed to familiarize learners with issues affecting Indigenous-settler relations across Canada today while exploring Indigenous histories, cultures, and perspectives

## 2.6 Harm Reduction

Harm reduction has been defined as “policies, programmes and practices that aim to minimise negative health, social and legal impacts associated with drug use, drug policies and drug laws. Harm reduction [...] focuses on positive change and on working with people without judgement, coercion, discrimination, or requiring that they stop using drugs as a precondition of support.”<sup>103</sup> Although most often associated with the use of illicit (non-medical or unregulated) substances, harm reduction approaches can also be applied to any behaviour that increases risk of adverse health, social, or legal consequences for an individual, including alcohol use.<sup>104</sup>

At its core, a harm reduction approach to alcohol use supports any steps taken by patients to improve their health and well-being, and seeks to meet patients “where they are at” in terms of interest in and ability to change their alcohol use.<sup>104</sup> Although it is understood that the only way to fully avoid all negative

consequences associated with alcohol use is abstinence, it is also recognized that not all patients are able or have a goal to discontinue or substantially reduce their alcohol use.<sup>104</sup> Thus, harm reduction involves mutual trust. It requires the care provider to set aside prejudice and permit marginalized persons to express their own principles of what it means to live the life they want to lead. Most importantly, it means that the patient can trust that their care team will not abandon them, even if they make decisions contrary to the guidance from their care team.

In circumstances in which a patient expresses interest in reducing alcohol consumption or alcohol-related harms rather than abstinence, clinicians can promote strategies to minimize alcohol-related harms rather than presenting abstinence from alcohol as the only desirable outcome of treatment (see [Setting Patient-Centred Treatment Goals](#)).

**Harm reduction strategies could include:**

- Promoting safer alcohol use strategies (e.g., reducing drinking—total consumption or drinking days per week, avoiding drinking and driving, reducing use of non-beverage alcohol)
- Optimizing engagement and retention in care
- Connecting patients with resources to address inequities in the social determinants of health (e.g., housing, legal services, financial assistance, employment programs)<sup>105-108</sup>

For some patients, a reduction in drinking can lead to clinically significant improvements in health and quality of life,<sup>109-111</sup> while for others, treatment goals can change from reduced drinking to abstinence over time with continued engagement in care.<sup>108</sup> This guideline also recognizes the growing body of evidence supporting managed alcohol programs as a harm reduction approach for individuals with severe AUD (see [Managed Alcohol Programs](#)).

## 2.6.i Indigenous Harm Reduction

An Indigenous approach to harm reduction recognizes the social and systems-level factors that impact alcohol use and alcohol-related harms among Indigenous peoples. This involves care providers personally engaging with the realities of structural racism and its impacts on their patients at an individual level, as well as critically reflecting on and working toward dismantling their own prejudices. In addition, clinicians should aim to work in partnership with their patients, understanding that the health system has been a site of significant harm for many Indigenous people and endeavouring to mitigate the power dynamic between provider and person seeking care. Indigenous harm reduction practices are imbued with Indigenous knowledges, values, and concepts of wholistic and relational wellness, and are not focused on individuals' alcohol use behaviours.

### Characteristics of Indigenous harm reduction

**Decolonizing**—goes beyond addressing individual behaviours and interrogates the neo-colonial systems and structures that shape and constrain the lives of Indigenous peoples by centering power and control in places where it has been systematically removed. In the context of substance use care, this involves providing services that are community-led, peer-led, trauma- and violence-informed, and culturally safe

**Indigenizing**—supporting programs and policies that are grounded in Indigenous knowledges, traditions, teachings, ceremonies, land, and languages

**Holistic and wholistic**—creating the conditions in which Indigenous peoples can be mentally, physically, emotionally, and spiritually well by addressing social determinants of health including housing, education, cultural practices, and other psychosocial supports

**Inclusive**—actively opposing “hierarchies of worthiness” imposed by colonial value structures. This involves respectful and non-judgemental care regardless of age, gender, sexuality, literacy levels, socioeconomic status, criminal backgrounds, spiritual belief, and alcohol and other substance use behaviours

**Innovative and evidence-based**—combining the best of Indigenous and mainstream approaches into effective and culturally grounded care

From the [Canadian Aboriginal AIDS Network](#)<sup>112</sup>

For further information, see [Indigenous Harm Reduction = Reducing the Harms of Colonialism](#) developed by the Canadian Aboriginal AIDS Network and the Interagency Coalition on AIDS and Development. Additionally, BC's First Nations Health Authority (FNHA) has developed a fact sheet on [Indigenous Harm Reduction Principles and Practices](#) which may be useful.



## 2.7 Recovery and Self-defined Wellness-Oriented Care

The continuum of care for AUD includes care planning and services oriented toward recovery and self-defined wellness. This guideline suggests adoption of the United States-based SAMHSA's [Working Definition of Recovery](#) as an overarching framework and for the purpose of developing patient-centred recovery and wellness-oriented treatment plans: “A process of change through which individuals improve their health and wellness, live a self-directed life, and strive to reach their full potential.”<sup>113</sup>

Those seeking recovery and wellness require understanding, support, and referral to appropriate services to achieve their goals, which may include abstinence for some patients, while for others, goals may involve reducing use or safer use. In some cases, patient-identified goals may not be directly related to alcohol use, such as improved health and wellness; having a safe and stable place to live; finding a sense of purpose through volunteerism, educational or employment activities; strengthening relationships with family and friends; or building social support networks.<sup>113</sup> Acknowledging and validating how individuals choose to define their recovery and wellness is an important component of this care. Recovery and wellness-oriented care strives to respect the choices, autonomy, dignity, and self-determination of individuals in defining their personal recovery goals and pathway.<sup>114</sup> There are multiple pathways to recovery and the journey may be more significant than the destination. Recovery and self-defined wellness-oriented care emphasizes holistic, client-centred, and strengths-based approaches and can encompass a spectrum of both abstinence-oriented and harm reduction management strategies.<sup>114</sup>

There is a diversity of recovery-oriented services that can provide additional care, support, and guidance to individuals and families affected by AUD in a manner that is complementary to the clinical management approaches delivered in primary care. This guideline emphasizes the importance of establishing functional referral networks and streamlined communication pathways between these two sectors as part of a broader strategy to build an integrated continuum of substance use care in each province and territory across Canada.

## 2.8 Integrated Continuum of Care

Alcohol use disorder is understood to be potentially chronic and relapsing. This underscores the importance of using a continuum of care approach, which includes risk reduction counselling, evidence-based pharmacotherapies, psychosocial treatment and interventions, culturally-specific services, and recovery and wellness-oriented support services. Individuals with AUD may access multiple approaches of varying intensity along this continuum of care to reduce harm, improve health and quality of life, and support long-term recovery and self-defined wellness.

This guideline supports the use of a stepped care and integrated approach, in which treatment options are continually adjusted to meet changing patient needs, circumstances, and goals. Recovery from moderate to severe AUD is rarely a linear process. A stepped care approach may include treatment intensification, transitions between different treatment options, and strategies to de-intensify treatment at the patient's discretion. Patients can opt to re-initiate pharmacotherapy, psychosocial treatment, or recovery-oriented supports at any time if their needs, goals, or circumstances change.

Primary care providers and care teams should ensure that patients with AUD and their families are aware of the range of community-based and, where relevant, specialist-led programs and services that are available to them, and regularly assess interest or readiness in accessing these services. To support continuity of—and transitions in—care across the continuum, primary care providers and care teams should establish fully functioning referral pathways. Clinicians should provide a clear explanation to patients regarding the reason for any referrals and offer additional support to ensure a successful referral. This may be particularly important for patients who have more complex health and social needs. Establishing protocols for communication and sharing information, with the patient's consent, between the primary care team and referral partners is strongly encouraged.

## 2.8.i Longitudinal Care Model

Traditionally, approaches to care and management of AUD have emphasized short-term and high-intensity treatment; for example, referring patients to inpatient withdrawal management or inpatient treatment programs without a plan for ongoing care after discharge or program completion. In recent years, there has been increased recognition that longitudinal care, meaning proactive efforts to continue care following the acute treatment phase, allows patients to sustain positive achievements toward their treatment goals. Continuous, longitudinal care has been shown to improve health outcomes in other chronic health conditions (e.g., diabetes, hypertension, heart disease), yet is not commonly practiced in the management of substance use disorders.<sup>115</sup> A pre-existing therapeutic relationship (or the development of one over time) can improve engagement and long-term retention in care.<sup>116</sup> An established relationship informed by trust and respect is critical for engaging people who have experienced trauma—who make up a significant proportion of people with AUD.

## 2.9 Comprehensive Health Management

As is the standard of care for any complex or chronic medical condition, all primary care clinicians and care teams should provide comprehensive health management to patients with AUD. By definition, this includes, but is not limited to: providing non-judgmental support and advice; assessing motivation and exploring barriers to change; developing and regularly reviewing a treatment and wellness plan with the patient; developing and strengthening stress management skills; and providing referrals to specialized medical care, recovery support, and social services when requested or appropriate.<sup>117</sup>

Management of AUD in primary care also permits the provision of more comprehensive care, which may include, but is not limited to: screening and clinical management of concurrent substance use and mental health disorders, comorbid medical conditions and alcohol-related sequelae (e.g., liver disease, gastrointestinal disorders, cardiovascular disease, dementia), preventive health care (e.g., vaccinations, general health screening), sexual and reproductive health services (e.g., sexually-transmitted infection screening, contraceptive

counselling, family planning), chronic disease management (e.g., arthritis, diabetes, cardiovascular disease), and referrals to specialist care.

## 2.10 Family and Social Circle Involvement in Care

This guideline uses the term “family” to encompass all relationships that are important to the patient, which may include romantic partners, close friends, and other people of significance who may or may not be legally recognized as family. Family members can have an important role as partners in an individual patient’s care, and this guideline recommends the inclusion of family members in decision-making processes and care at all levels, when deemed appropriate by patients and their care teams. Research has shown that families can have a pivotal role in improving treatment outcomes and sustaining benefits of treatment among youth and adults with AUD by providing additional support and structure and promoting resilience.<sup>118-121</sup> If a patient determines family involvement would be a positive element in their treatment plan, clinicians are encouraged to educate family members about available treatment options and resources and provide as much patient-specific information as possible within the boundaries of confidentiality requirements.

As with all medical care, confidentiality requirements must be met when treating individuals with AUD. This includes maintaining confidentiality from family members unless patients have granted consent for their medical information to be shared with their family.<sup>122</sup> Health care providers should avoid making assumptions about privacy and routinely ask patients if they prefer to include family members or friends as supportive partners in their care. If aspects of care are being kept confidential from family members, the challenges and logistics of this should be discussed with the patient. While information about a person cannot be shared with family members without a patient’s consent, family members can share relevant information with health care providers without violating that patient’s privacy or confidentiality—although the family member should be made aware that this information may need to be shared with the patient. A clinician can also provide education and support to a family without disclosing any information about an individual.

It is important to note that, in some cases, family involvement may not be in the best interest of the patient. Factors such as partner or parental substance use, familial abuse and violence, or dysfunctional family relationships can act as barriers to engagement and retention in treatment as well as to achieving long-term recovery.<sup>118-121</sup> Family member involvement should not replace adequate medical care. Although families often take on significant caregiving roles, they usually receive little or no training or orientation and may lack information regarding AUD and treatment.<sup>123</sup> Patients, provided they are capable decision-makers, should be given full discretion on whether and how they wish to include family members in their care, and if they opt not to involve family members, this decision should be respected.

In the case of youth (aged 11–25), parental participation in treatment should be actively encouraged, if appropriate, but is not required and is dependent on patient preference. Family members and caregivers should be supported with sufficient education and information about alcohol use and AUD. A family history should be taken, when possible, to identify any mental health or substance use issues requiring treatment in the youth's family, recognizing these may influence the youth's alcohol use through modelling, creating stressors for the youth, or reducing the family member's ability to provide support for the youth with AUD. It should also be noted that, like adults, not all youth have healthy or positive relationships with their family members. Decisions to involve family members in care should be guided by the patient's wishes and an understanding of the family dynamic.

Regardless of their level of involvement in a patient's care, family members and caregivers often require support for their own health and wellness. Several resources exist for family members impacted by alcohol and AUD, including [Al-Anon and Alateen Family Groups](#), [SMART Recovery for Family and Friends](#), and [Families for Addiction Recovery](#). Family members can also be referred to external specialist-led and community-based services and supports. Clinicians should be mindful of any concerns that patients may have about privacy, confidentiality, or perceived conflicts of interest if patients and family members are referred to the same specialist-led or community-based programs. [The Canadian Medical Protective Association](#) provides advice to physicians for a variety of medico-legal issues including confidentiality and family member involvement in care.

# 3 Screening, Diagnosis, and Brief Intervention

Screening, diagnosis, and brief intervention are the beginning of the AUD treatment pathway. Screening identifies individuals who consume alcohol at high-risk levels and should undergo a diagnostic interview for AUD. Diagnosis allows for the formal identification of high-risk drinking and mild, moderate, and severe AUD in order to facilitate early intervention and connection to care. Brief intervention supports behavioural change to reduce or discontinue alcohol consumption through brief, time-limited counselling sessions based on motivational interviewing. Brief intervention should be offered alongside other psychosocial and pharmacological treatment interventions for individuals diagnosed with AUD.

Health care providers and service operators are encouraged to develop clinical pathways and processes that support screening and early intervention for individuals who meet criteria for drinking above low-risk limits, along with a plan for required diagnostic follow-up and treatment for individuals who are diagnosed with AUD.

## 3.1 Providing Education on the Continuum of Alcohol-related Risks to Patients

This guideline endorses the adoption and use of [Canada's Guidance on Alcohol and Health](#)<sup>8</sup> as an educational resource and discussion tool in primary care practice. *Canada's Guidance on Alcohol and Health* was released in 2023 as an update to the *Low-Risk Alcohol Drinking Guidelines*<sup>124</sup> published in 2011 following new evidence on alcohol-related morbidity, mortality, and social harms. The guidance introduces significant changes to the thresholds for low- and high-risk drinking and removes distinctions by age and sex.

Research on the *Low-Risk Alcohol Drinking Guidelines* shows that public awareness and knowledge of these guidelines was low. Several provincial and national surveys of the general public have reported that fewer than 20% of respondents were aware that the *Low-Risk Alcohol Drinking Guidelines* existed, and fewer still

were able to correctly identify standard drink sizes or recall age- and sex-specific limits for low-risk drinking.<sup>125-129</sup> While some studies suggest that mass media campaigns aimed at increasing knowledge of national low-risk drinking guidelines can lead to short-term reductions in alcohol consumption,<sup>130,131</sup> others have found that without personalized context, some individuals may perceive low-risk guidelines as not realistic or relevant to their lives, particularly when they are drinking above low-risk limits.<sup>125,132</sup>

Primary care providers can play an important role in promoting awareness about the continuum of alcohol-related risks by providing patients with information and education about *Canada's Guidance on Alcohol and Health*, as well as working with patients to understand in which risk zone their alcohol use places them and the implications for their health and daily life. Education about the risks of alcohol can encourage people to adopt healthier and safer behaviours (i.e., to move toward a lower risk drinking zone along that continuum).

Clinicians should be mindful that some patients may experience stigma when asked questions about alcohol use or may consider these questions as culturally taboo, especially without a pre-existing relationship and clear rationale for asking. Introducing the topic in a general and conversational way can help build rapport and comfort in talking about personal use during the subsequent steps in the screening and brief intervention pathway. Seeking the patient's consent and providing context prior to asking screening questions can foster trust and comfort. For example:

*"I routinely discuss the health effects of alcohol with all my patients.  
Would it be alright for us to talk about this now?"*

If the patient is open to the discussion, asking exploratory, open-ended questions on alcohol use can help facilitate respectful, productive conversations.

Examples:

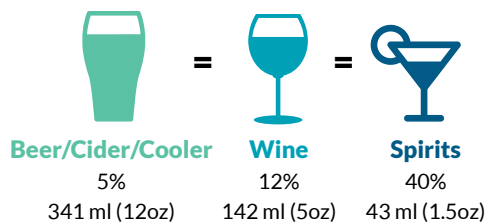
*"How does alcohol fit in your life?"*

*"What kind of relationship do you have with alcohol?"*

Clinicians can gauge the patient's interest in learning more about the effects of alcohol and risk levels and decide whether continued discussion would be appropriate and beneficial. Further guidance and examples for initiating these conversations is in [Appendix 2.1](#).

### 3.1.i Overview of Canada's Guidance on Alcohol and Health

**In Canada, a standard drink is 17.05 ml or 13.45 g of pure alcohol**



*Canada's Guidance on Alcohol and Health* provides people living in Canada with accurate and current information about the risks and harms associated with the use of alcohol. The guidance is intended to help people make well-informed decisions about their alcohol consumption.

*Canada's Guidance on Alcohol and Health* reflects conclusions drawn from global evidence reviews, mathematical modelling of the lifetime risk of death and disability for various levels of alcohol consumption, and consultations with the public and experts. Mathematical modelling revealed that 2 standard drinks per week is associated with a 1 in 1,000 mortality related to an alcohol condition, while 6 standard drinks per week is associated with a 1 in 100 risk. Observational cohort studies have found that average long-term alcohol consumption levels as low as 1 or 2 standard drinks per day are directly or indirectly linked to increased risk of at least 8 different types of cancer (oral, pharynx, larynx, esophageal, liver, breast, colon and rectal cancers) as well as numerous other serious medical conditions (e.g., epilepsy, hemorrhagic stroke, cardiac dysrhythmias, liver cirrhosis, and hypertension).<sup>133-139</sup> In addition, there are a number of serious medical conditions directly attributed to long-term alcohol consumption, including AUD, alcohol-related psychosis, nervous system degeneration, polyneuropathy, myopathy, cardiomyopathy, gastritis, liver diseases (e.g., hepatitis), and pancreatitis.<sup>124,133,137-139</sup>

**Canada's Guidance on Alcohol and Health models the risk for many alcohol-related conditions and outcomes, including cancer, heart disease, stroke, liver disease, hypertension, and unintentional injuries.**



Therefore, there is a continuum of risk from negligible to low ( $\leq 2$  standard drinks per week), through moderate (3–6 standard drinks per week) to high ( $\geq 7$  standard drinks per week), with increasingly higher levels of risk with every additional drink.

Risk zone	Number of standard drinks per week
No risk	0
Low risk	1 – 2
Moderate risk	3 – 6
High risk	7 – +

On any single drinking occasion, the risk of acute outcomes such as unintentional injuries and violence is strongly associated with consuming larger amounts of alcohol. The risk of negative outcomes begins to increase with any consumption, and with more than 2 standard drinks, most individuals will have an increased risk of injuries or other problems. Binge drinking, usually defined as consuming 5 standard drinks or more for men, or 4 standard drinks or more for women in one drinking episode, is a risk factor for death from any cause, including unintentional injuries, violence, heart disease and high blood pressure, inflammation of the gastrointestinal system, and for the development of an alcohol use disorder.

*Canada's Guidance on Alcohol and Health* also makes recommendations for specific populations and scenarios in which either abstinence from alcohol use is advised, including during pregnancy and the pre-conception period, and for those who are breastfeeding.<sup>8</sup> The Canadian Coalition for Seniors' Mental Health (CCSMH) has published lower-risk drinking limits specifically for older adults.<sup>140</sup>

In Canada, among persons aged 15 and older, 20% do not drink alcohol, 21% usually consume less than 2 standard drinks per week; 17% consume 3–6 standard drinks per week on average and 40% usually consume more than 6 standard drinks per week.<sup>141,142</sup> Thus, over half of all alcohol consumed in Canada is in excess of levels deemed low risk.

To support discussions about *Canada's Guidance on Alcohol and Health*, the Canadian Centre on Substance Use and Addiction (CCSA) has created a number of patient education and decision-making [tools](#).

### 3.1.ii Section Summary and Recommendation

This guideline strongly recommends that clinicians provide education to their patients about *Canada's Guidance on Alcohol and Health* to both enhance awareness and knowledge of alcohol use among their patients and **as an introduction to alcohol use, prior to screening**. Although research evidence is limited, increased awareness and knowledge of safer alcohol consumption guidelines may lead to reductions in alcohol consumption,<sup>130,131</sup> particularly when the person has expressed an interest in learning more about the harms of alcohol, is interested and able to change their personal habits, and has support from other caregivers, family members, or community.

## Recommendation 1

**When appropriate, clinicians should inquire about current knowledge of and offer education to adult and youth patients about Canada's Guidance on Alcohol and Health, in order to facilitate conversations about alcohol use.**

LOW Quality of Evidence

STRONG Recommendation

### Remarks

- *Canada's Guidance on Alcohol and Health* provides a continuum of risk based on weekly consumption and single occasion consumption.
- Practicing cultural safety and humility<sup>h</sup> are critical when talking to Indigenous patients and families about alcohol use. Widespread harmful stereotypes regarding Indigenous peoples and alcohol have contributed significant harm to Indigenous people within and outside of healthcare contexts. Committing to an ongoing practice and learning of cultural humility and safety can strengthen relationships with Indigenous patients. It is important to be mindful of how you approach this topic in conversation with Indigenous patients.
- Clinicians should tailor their approach and language based on their relationship with each patient and each patient's circumstances. Examples of how to start conversations about alcohol use can be found in [Appendix 2: Screening and Diagnosis](#).
- The quality of evidence for this recommendation was rated as low due to the limited research evidence regarding the use of Canada's previous *Low-Risk Alcohol Drinking Guidelines* as an educational tool in clinical practice and the absence of research evidence for *Canada's Guidance on Alcohol and Health* (released January 2023).
- The strength of this recommendation was rated as strong based on working group consensus, despite limited research evidence. It is the consensus of the committee that all patients could potentially benefit from conversations about alcohol use with their health care provider and utilizing *Canada's Guidance on Alcohol and Health* may facilitate increased awareness and knowledge of lower-risk alcohol use limits.

<sup>h</sup> See [Indigenous Cultural Safety](#) and [Indigenous Harm Reduction](#) in this document for more information on integrating cultural safety and humility into clinical practice.

## 3.2 Alcohol Use Screening

Despite its high prevalence in primary care and other clinical settings, alcohol use that poses a risk for developing negative health consequences or AUD often goes unrecognized and untreated.<sup>143</sup> Implementation of routine and universal alcohol use screening in primary care practice has increasingly been advocated for as an important public health strategy for early identification of high-risk alcohol use and secondary prevention of AUD.<sup>144-146</sup>

### Definition of high-risk alcohol use in this guideline:

- **A pattern of alcohol use associated with the development of negative physical and/or mental health consequences. Adverse social consequences are common.**
- **Indicated by an AUDIT score  $\geq 16$  or AUDIT-C score  $\geq 8$ .**

The underlying rationale of universal screening is to capitalize on patterns of practice that are already in place as well as the longitudinal model of care in the primary care setting. Patients can be routinely asked about alcohol use during new client intakes, general assessments, annual preventive screening, and in specific disease management clinics (e.g., hypertension, diabetes). Thus, screening could occur when alcohol use is not the primary reason for presentation, facilitating early intervention and connection to care among patients not actively seeking treatment for alcohol-related issues or concerns. Early intervention is crucial, as **screening alone does not improve patient outcomes.**

Establishing trust and safety in these initial conversations is particularly important for patients who may otherwise tend to underreport substance use, such as pregnant individuals, youth, older adults, people working in safety-sensitive positions, or patients with co-occurring substance use disorders where alcohol use may be associated with greater risk of harm. For all patients, clinicians may want to continue checking for consent prior to asking screening questions. For example:

*“Do you mind if I ask you some questions about how much you drink?”*

### 3.2.i Screening Adult Patients

A number of standardized alcohol use screening instruments have been validated in a range of clinical care settings, including the Alcohol Use Disorders Identification Test (AUDIT), the condensed AUDIT-Consumption (AUDIT-C) test, and the Cut-down, Annoyed, Guilty, Eye Opener (CAGE) questionnaire (see [Appendix 2: Screening and Diagnosis](#)).<sup>i</sup> Provider-level barriers, including time constraints, lack of familiarity with the instruments, and the requirement to calculate item and overall scores have been cited as impediments to the

uptake and use of such screening tools in primary care settings. In response to these barriers, brief validated screening tools have been developed. An approach specifically tailored for the primary care setting is the Single Alcohol Screening Question (SASQ), as it takes minimal time to administer, is easily recalled, and requires no scoring.<sup>148</sup> Likewise, the AUDIT-C is comprised of only the first 3 questions of the AUDIT questionnaire and has been shown to be convenient and effective in a primary care setting.<sup>149</sup> Non-validated screening tools and those with poor sensitivity and specificity should be avoided.<sup>150</sup>

**Throughout this guideline, systematic reviews and meta-analyses are described with this notation:**

**N = [number of studies],**

**n = [number of participants]**

#### Box 1. Terminology Used to Assess Screening Tools

<b>Sensitivity</b>	The proportion of individuals correctly identified as having the condition, or “true positives.”
<b>Specificity</b>	The proportion of individuals correctly identified as not having the condition, or “true negatives.”
<b>Remarks:</b> Sensitivity and specificity can vary according to the cut-point used for the scale, the population being assessed, the setting, and the experience of the assessor. Sensitivity and specificity scores of 0.75 or 75% or higher are generally considered to be useful. <sup>151</sup>	

i The validity studies cited in this guideline were in English. The AUDIT and AUDIT-C have been translated into many other languages and have shown good performance and reliability.<sup>147</sup>

### 3.2.i.1 Single Alcohol Screening Question

The SASQ is typically structured around sex- and age-specific cut points that are associated with high-risk drinking or AUD. To normalize discussions about alcohol use and support disclosure, patients are asked the following question:

*“In the past year, how often have you consumed more than 4 drinks (for adult women) or 5 drinks (for adult men) on any one occasion?”<sup>k</sup>*

Any response greater than “never” or “zero times” to the question below would be considered a potential indication of high-risk drinking or AUD. A review of validation studies for this SASQ (N [number of studies] = 6, n [number of participants] = 44,244) found a sensitivity range of 0.71 to 0.92 (95% CI range, 0.65 to 0.98) and specificity range of 0.60 to 0.91 (95% CI range, 0.55 to 0.95) for detecting AUD.<sup>153</sup> For detecting risky drinking<sup>l</sup>, studies have found sensitivities of 0.82-0.96 and specificities of 0.58-0.79.<sup>154-156</sup> These studies were conducted in the US in primary care settings. Due to its brevity and ease of use, systematic reviews have concluded that this is a valid option in clinical settings where time and patient interactions are limited.<sup>148,157</sup> A study of combinations of screening tools found that a brief screen followed by a longer, validated tool such as the AUDIT or CAGE provided the optimal approach for accuracy and efficiency.<sup>148</sup> The SASQ does not take into account frequency and other factors (e.g., drinking patterns and behaviours), therefore if the patient screens positive, it is recommended that:

**SASQ should be followed by another screening tool (e.g., AUDIT, AUDIT-C, CAGE) to increase accuracy and specify risk levels.**

- j There is little research on screening tools among gender diverse (e.g., transgender, non-binary) individuals. Clinicians can adjust screening for their patients based on various individual factors, including mass, biological (sex-related) factors (e.g., alcohol pharmacokinetics, hormone levels), and psycho-sociocultural (e.g., gender-related) factors.<sup>152</sup>
- k The cut-points of 4 standard drinks for women and 5 standard drinks for men per day are most commonly used in single question validation studies for AUD and are also used by the US National Institute on Alcohol Abuse and Alcoholism (NIAAA). These numbers correspond to the definition of binge drinking in *Canada's Guidance on Alcohol and Health* or heavy drinking for the NIAAA. Previous research indicated differing levels of risk in women versus men due to sex differences in metabolism.<sup>124</sup>
- l In these studies, risky drinking was defined as 5 drinks in a day or 14 drinks in a week for men and 4 drinks in a day or 7 drinks in a week for women at any time in the last 30 days.

### 3.2.i.2 AUDIT-Consumption (AUDIT-C) Tool

The condensed AUDIT-C consists of 3 questions about alcohol consumption<sup>149</sup>:

1. *“How often do you have a drink containing alcohol?”*
2. *“How many units of alcohol do you drink on a typical day when you are drinking?”*
3. *“How often do you have six or more drinks on one occasion”*

The AUDIT-C is scored on a scale of 0 to 12 and has been validated for the identification of risky drinking<sup>1</sup> or AUD (see [Box 11](#) for scoring and interpretation). Validation studies defined the comparison standards based on self-reported alcohol consumption in the past month, standardized diagnostic interview for AUD, and AUDIT score. A 2007 review indicated that using a cut-point of 4 to identify either risky drinking or AUD, the sensitivity ranges from 0.76 to 0.99 and specificity ranges from 0.66 to 0.98 in the general population, primary care, and veterans.<sup>147</sup> Based on data from various cut-points, the authors suggested that a cut-point of 3, rather than 4, performed better to identify risky drinking in women. Scores can also be used to identify low-, moderate-, and high-risk drinking categories.<sup>158</sup> Additional details are provided in [Appendix 2.3](#). Individuals who screen positive for high-risk drinking on the AUDIT-C should be offered further assessment and a diagnostic interview for AUD.

### 3.2.ii Screening Indigenous Peoples

Before discussing alcohol use with Indigenous people, clinicians should be aware of the systemic and ongoing impacts of colonization on Indigenous peoples that have resulted in the ongoing stereotyping and resultant racism toward Indigenous peoples.<sup>159-161</sup> This systemic racism has been widely experienced in health care settings and impeded timely access to health care, resulting in poorer health outcomes. Due to ongoing racism and stigma surrounding Indigenous people and alcohol and other substance use,<sup>71-73</sup> Indigenous people are less inclined to disclose alcohol or other substance use compared to their non-Indigenous counterparts to avoid further discrimination.<sup>162</sup> To combat these impacts, clinicians must commit to learning more about cultural safety and humility (see [Indigenous Cultural Safety](#)) and embed it into clinical practice in order to minimize potential harms when discussing and screening for alcohol use.

**Clinicians should seek the patient's consent and provide context before asking about alcohol use and consider establishing a longitudinal relationship with the patient before screening for alcohol use.**

Guidelines recommend routine and universal screening for alcohol consumption for Indigenous peoples.<sup>163,164</sup> While the AUDIT, AUDIT-C, CAGE, and CRAFFT are commonly used tools to screen for alcohol use among Indigenous peoples in Canada, the United States, Australia, and New Zealand, few studies examining the accuracy and validity of these tools for Indigenous peoples have been conducted.<sup>165</sup> Regardless of the screening tool selected, clinicians should consider the common barriers that Indigenous peoples may experience in regard to screening. Language barriers may be present when screening for alcohol use, and some Indigenous peoples may prefer to have an interpreter present during their visit.

### 3.2.iii Screening Youth Patients

For youth, there are validated screening tools available, including the NIAAA screening tool, AUDIT, AUDIT-C, and the six-question Car, Relax, Alone, Forget, Friends, Trouble (CRAFFT) instrument, which is specifically for screening youth aged 12–21 (see [Box 13](#)). A simplified 1- or 2-question screening approach may be preferred in primary care due to brevity and ease of recall.<sup>166-168</sup> A 2019 meta-analysis (N = 33 studies above quality threshold<sup>m</sup>, n = 190,362) found that alcohol use screening tools<sup>n</sup> have a sensitivity of 0.98 (95% CI: 0.95 to 0.99) and a specificity of 0.78 (95% CI: 0.74 to 0.82) for youth under the age of 24.

m *A priori* quality thresholds were used to determine which studies should be included in full data abstraction. To be considered above the quality threshold, a study's index test was required to have: a predictive value above 0.7, or an internal consistency above 0.8, or a test-retest value above 0.7.

n The screening tools included in this meta-analysis include: AUDIT; AUDIT-C; binge drinking; CAGE; Concern/cut-down, Under influence, Guilt, and Eye-opener (CUGE); CRAFFT; Fast Alcohol Screening Test (FAST); frequency item; heavy episodic drinking frequency item; modified AUDIT; modified Tolerance, Worried, Eye-opener, Amnesia, K/Cut Down (TWEAK); Problem Oriented Screening Instrument for Teenagers (POSIT); quantity item; quantity X frequency item; Rapid Alcohol Problem Screen-Quantity Frequency (RAPS4-QF); Riding with intoxicated driver, Unable to stop, Family/friends, Trouble, Cut-down (RUFT-Cut).

Specifically, single-item screening tools focused on frequency of alcohol use (n = 18; average sensitivity: 1.00, average specificity: 0.84) have a greater number of validation studies supporting their use compared to single-item screening tools focused on quantity of alcohol use (n = 10; average sensitivity: 0.96, average specificity: 0.91), but the majority of data for each of these measures was based on a single large epidemiological study.<sup>169</sup>

### **3.2.iii.1 National Institute on Alcohol Abuse and Alcoholism (NIAAA) Youth Screening Tool**

The United States NIAAA developed a two-question tool for screening youth aged 11–18 years that consists of the following questions<sup>170</sup>:

1. *“Have any of your friends consumed alcohol in the past year?”*
2. *“Have you consumed any alcohol in the past year?”*

These questions were empirically derived from extensive analyses of national survey data and have the strongest evidence base for predicting current or future alcohol-related problems in youth.<sup>170</sup> For youth aged 11–14 (Grades 6–8), it is recommended to first ask about alcohol use among friends as a less intimidating introduction to the topic, followed by personal use questions (i.e., question 1 then 2). For youth aged 14–18 (Grades 9–12), ask the personal use question first.<sup>171</sup>

To assess risk and triage youth appropriately, ask all youth aged 11–18 years who screen positive for personal use (“yes” to question 2) to estimate the number of days they have consumed alcohol over the past year.<sup>172,173</sup> Self-reported drinking days that exceed age-specific thresholds signal that the patient may have an increased chance of developing alcohol-related problems, including AUD.<sup>174</sup> Further information on interpretation and follow-up is provided in [Appendix 2.3](#).



Table 2. Age-Specific Thresholds for High Risk Using the NIAAA Youth Screening Tool

Age	High-risk threshold for past year drinking
11 years	1 day
12–15 years	6 days (about every other month)
16 years	12 days (about monthly)
17 years	24 days (about twice monthly)
18 years	52 days (about weekly)

Prospective evaluations of the NIAAA tool incorporating these age-specific cut-points have concluded that it is an accurate and reliable method for screening and triaging youth for more intensive interventions in primary care settings.<sup>175,176</sup> However, these studies also noted the advantages of having a simplified version of the tool that could be used to stratify youth of any age into lower- versus higher-risk categories.

To date, several studies have investigated a simplified version of the NIAAA tool for triaging youth based on current or future risk of alcohol-related harms. A 2014 diagnostic accuracy study (n = 525) conducted in an urban primary care setting found that utilizing a threshold of  $\geq 2$  drinking days per year for youth aged 12–17 (n = 525) conferred high sensitivity (96%; 95% CI: 0.83 to 1.00) and specificity (85%; 95% CI: 0.82 to 0.88) for identifying individuals who met DSM-5-TR criteria for AUD through diagnostic interview.<sup>175</sup> The simplified NIAAA screening tool was subsequently evaluated in a 2016 diagnostic accuracy study conducted in 6 rural primary care clinics, where researchers determined a threshold of  $\geq 3$  drinking days per year had a 91% sensitivity and 93% specificity for detection of AUD among youth aged 12–17 (n = 942) and a positive predictive value<sup>o</sup> of 44% and negative predictive value<sup>p</sup> of 99%.<sup>176</sup> Further research is required to improve the precision and accuracy of cut-points for the risk-based triage of youth and, as illustrated by findings that cut-points may differ between urban and rural

- o Positive predictive value reflects the proportion of subjects with a positive test result who truly have the outcome of interest
- p Negative predictive value reflects the proportion of subjects with a negative test result who truly do not have the outcome of interest.

settings,<sup>176</sup> local context may play an important role. In the interim, using the age-specific cut-points for high-risk alcohol use as described in [Table 2](#) is advised.

### 3.2.iv Screening Pregnant Patients

Universal screening of all primary care patients allows for timely intervention prior to pregnancy and secondary prevention of maternal/parental<sup>q</sup> and fetal harms associated with alcohol use.<sup>177</sup> Research has suggested that patient self-reports are a valid measure of alcohol use during pregnancy<sup>178</sup>; however, clinicians should be sensitive to factors that may deter patients from providing accurate responses to screening questions, such as stigma and fear of child apprehension.<sup>179,180</sup> To address these concerns, it is crucial to establish rapport and trust before introducing the topic. Once comfort and trust have been established, then seek the patient's informed consent prior to screening. As part of the informed consent process, discuss the limits of confidentiality and their rights in accordance with the standards of medical practice.<sup>41,181,182</sup> For further guidance and strategies to support culturally safe care in Indigenous patients, see the Society of Obstetricians and Gynaecologists of Canada's (SOGC) [Consensus Guideline for Health Professionals Working With First Nations, Inuit, and Métis](#)<sup>183</sup> and the guideline's [Companion Piece](#).

Prior to screening, it is crucial to secure the patient's consent and to review confidentiality and other rights of the patient involved, congruent with the standards of medical practice.<sup>41</sup> **Clinicians should be aware that “duty to report” does not apply to prenatal alcohol or substance use,**<sup>184</sup> and thus, prenatal alcohol use should not be reported.

Alcohol use screening should be conducted at the first prenatal visit or during the first trimester, and as needed in subsequent visits.<sup>185</sup> Although not explicitly

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q While the majority of pregnant individuals identify as women, this term does not reflect the identities and experiences of all pregnant people, some of whom may not identify as women. This guideline uses gender-neutral language in pregnancy-related guidance to support inclusivity of sex- and gender-diverse patient populations. Asking patients how they choose to identify themselves and using their chosen pronouns (e.g., they/them/theirs, she/her/hers, he/him/his) is an important component of person-centred care.

validated for use in pregnant patients, the SASQ has been recommended as the first step in alcohol use screening in this population by the Society of Obstetricians and Gynaecologists of Canada<sup>185</sup> and the US Preventive Health Services Task Force.<sup>157</sup> As with non-pregnant patients, a simplified approach to alcohol use screening may be preferred in the prenatal care context. The general consensus among experts is that these questions are sufficiently sensitive and specific for identifying pregnant individuals who consume alcohol above lower-risk levels.<sup>177</sup> When combined with supportive, non-judgmental dialogue, the SASQ format—asking open-ended rather than yes or no questions and assessing alcohol use patterns over the past year—can encourage an open discussion about alcohol use, increase understanding of why the person may be drinking alcohol, and strategies to support the parent and reduce maternal/parental and fetal risks.<sup>185</sup> As well, individuals may be more likely to report pre-pregnancy or lifetime alcohol use, rather than alcohol use during pregnancy because of the risks and stigma involved in disclosure of the latter.<sup>177</sup> Further guidance on alcohol use screening during pregnancy can be found [online](#).

Individuals who disclose alcohol use during pregnancy should undergo further assessment to determine frequency and amount of alcohol consumption and to differentiate high-risk use from individuals with AUD (see [Diagnosis of Alcohol Use Disorder](#)). If alcohol use is likely to impact parenting, early referral and involvement of social work, with the patient's consent and participation, can greatly improve social outcomes.

### 3.2.v Screening Older Adults

Screening for alcohol use is recommended for all older adults (generally, individuals 65 years of age and older<sup>r</sup>). While Canadian data is not available, national survey data collected between 2015 and 2019 (n = 9,663) from the United States indicate that approximately 25% of older adults who reported accessing health care and consuming alcohol in the previous year were not asked about alcohol use by health care providers during health care appointments.<sup>186</sup> Screening is particularly important for older adults, as those who consume alcohol above lower-risk limits are at a greater risk of developing new or worsening existing comorbidities. This is, in part, due to age-related changes to the manner and rate of absorption, distribution, and excretion of alcohol in the body. In addition, older adults may be more susceptible to the effects of interactions between alcohol and prescription or unregulated drugs and generally do not metabolize medications as efficiently as younger adults, increasing the risk of drug–drug interactions at lower levels of alcohol consumption.<sup>140,187</sup>

In 2019, the Canadian Coalition for Seniors’ Mental Health published the [Canadian Guidelines on Alcohol Use Disorder Among Older Adults](#). They recommend that all older adults are screened for alcohol consumption at least annually (e.g., during an annual check-up) and at transitions of care (e.g., admission into a hospital).

Screening tools that can be used with older adults include the AUDIT, CAGE, Shortened Michigan Alcoholism Test–Geriatric version (SMAST-G), Comorbidity Alcohol Risk Evaluation Tool (CARET), and the Senior Alcohol Misuse Indicator (SAMI). More information on each of these tools can be found in the [CCSMH Guideline](#). Screening for alcohol use in older adults

**The SMAST-G, CARET, and SAMI were developed specifically for older adults.**

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<sup>r</sup> Aging has many dimensions, encompassing biological, psychological, social, and cognitive risk factors. Throughout this guideline, “older adult” refers to those 65 years of age and older. However, the guidance may be relevant for some individuals under 65 years of age, due to medical, psychological, and social contexts. Conversely, some individuals 65 years of age and older may be better suited to approaches used for adults under 65.

is recommended to take place in various clinical settings, including hospitals, rehabilitation facilities, home health care, community services, assisted living and long-term care facilities, and specialized programs. When screening older adults, clinicians should ensure that screening is age-appropriate, supportive, and accounts for memory impairment or cognitive decline.<sup>140</sup>

*Box 2. Indications for screening older adults*

**Clinicians should consider screening older adults for alcohol use more frequently if any of the following factors are present<sup>140</sup>:**

- Alcohol use exceeds lower-risk limits
- Patient exhibits or reports symptoms of AUD
- Family history of AUD
- Symptoms of anxiety or depression
- Caregivers express concern
- Significant life changes or transitions have occurred

### 3.2.vi Frequency of Alcohol Use Screening

Based on a 2018 meta-analysis (N = 11, n = 314,446), the US Preventive Services Task Force concluded that there is insufficient research evidence to recommend an optimal screening interval for alcohol use in adults and youth.<sup>146,188</sup> Some organizations, such as the US Department of Veterans Affairs, strongly recommend annual screening.<sup>189</sup> This is for reasons of convenience—alcohol screening can be combined with other components of a routine medical exam or preventive health screening—and to detect changes in an individual’s alcohol use patterns and behaviour, as these can change with life circumstances.

Where appropriate, screening for alcohol use more frequently may more accurately capture an individual’s alcohol consumption patterns. A 2020 study (n = 831) found that 39% of individuals did not have consistent drinking patterns across screening assessments conducted at baseline, 3-, 6-, and 12-months. Of those who had been identified as consuming alcohol at lower risk levels at baseline, 21% later screened positive for high-risk alcohol consumption at one or

more follow-up assessments. Predictors of transitioning from lower-risk drinking at baseline to a subsequent positive screen for high-risk alcohol use were being female, being 18–29 years old, and reporting 2 or more drinking days or heavy episodic drinking in the week prior to baseline assessment.<sup>190</sup>

### 3.2.vii Clinical Indications for Alcohol Use Screening

This guideline recommends universal screening of all adult and youth patients in primary care. However, there are several common clinical scenarios that should trigger alcohol screening regardless of whether or when a patient was last screened.

#### Box 3. Indications for Alcohol Screen

- Signs of intoxication or detection of alcohol on breath
- Before prescribing a medication known to interact with alcohol
- Patient reports prescribed or illicit use of opioids, benzodiazepines, or other substances
- Patients with chronic non-cancer pain
- Laboratory investigations show elevated liver enzymes (increased GGT, AST:ALT ratio > 2:1), or MCV > 96fL on CBC panels
- Patients who are pregnant or planning to become pregnant
- Recent or repeated physical trauma, burns, injuries, accidents, or falls
- Recent, historical, or recurrent psychological trauma or intimate partner or family violence
- Significant life event (e.g., death of spouse or family member, divorce)
- Signs of workplace dysfunction (e.g., unexplained time off, loss of employment)
- Behaviours that put the patient at risk of harm (e.g., high-risk gambling, unprotected sex, impaired driving)
- Suspected, diagnosed, or worsening health conditions that may be associated with alcohol use:
  - Depression
  - Anxiety
  - Insomnia
  - Seizures
  - Psychosis
  - Mania
  - Anemia
  - High blood pressure
  - Cardiovascular complications (e.g., arrhythmia)
  - Gout
  - Memory issues
  - Pancreatitis
  - Gastrointestinal disorders
  - Hepatitis, cirrhosis

s Abbreviations: GGT—gamma-glutamyl transpeptidase, AST—aspartate aminotransferase, ALT—alanine transaminase, MCV—mean cell corpuscular volume, CBC—complete blood count

Additionally, patients presenting to care because they are concerned about their alcohol use or suspect they have AUD can undergo a full diagnostic interview immediately.

### **3.2.viii Section Summary and Recommendation**

Based on known risks and harms of high-risk drinking and AUD, and the benefits of early identification, intervention, and treatment, this guideline recommends universal alcohol use screening for all adult and adolescent patients seen in primary care.

The committee endorses the use of a single alcohol screening question (SASQ) and AUDIT-C for adult patients (including pregnant individuals) and the NIAAA tool for youth. Simplified screening tools have several advantages in primary care,<sup>148</sup> while still achieving acceptable sensitivity and specificity for detection of high-risk drinking compared to more complex screening tools.<sup>148,156,191-193</sup>

There is a lack of evidence regarding optimal screening–rescreening intervals in adults and youth. Given the advantages of early detection and intervention to reduce or prevent alcohol-related harms, it is the consensus of this committee routine screening is beneficial.

## Recommendation 2

All adult and youth patients should be screened routinely for alcohol use above low risk.

MODERATE Quality of Evidence

STRONG Recommendation

### Remarks

- Clinicians should seek the patient’s consent and provide context before asking about alcohol use and consider establishing a longitudinal relationship with the patient before screening for alcohol use.
- Screening alone does not improve outcomes. As a standard component of screening, all patients should be provided with individually tailored feedback about their results, regardless of the screening tool used.
- Patient-specific circumstances may indicate more frequent screening (e.g., older adults [ $> 65$ ], adolescents [ $< 18$ ], individuals with a history of substance use disorder, and individuals with a family history of alcohol use disorder, in addition to the [Clinical Indications for Alcohol Use Screening](#)).
- Individuals who screen positive for high-risk drinking should be offered a diagnostic interview for AUD and further assessment to determine a treatment approach.
- The quality of evidence for this recommendation was rated as moderate based on systematic reviews and diagnostic accuracy studies that demonstrate screening tools accurately identify individuals who consume alcohol at high-risk levels. There is insufficient research evidence to recommend an optimal screening interval for alcohol use in adults and youth; however, some public health organizations recommend screening at least annually.
- The strength of this recommendation was rated as strong based on quality of evidence, working group consensus, cost-effectiveness, and the accuracy of available screening tools.

### 3.3 Diagnosis of Alcohol Use Disorder

Patients who screen positive for high-risk drinking should undergo a diagnostic interview for AUD using the DSM-5-TR criteria (see [Table 11](#)). Confirmation or exclusion of AUD and an assessment of AUD severity and the patient’s risk of complications determine subsequent steps in the treatment pathway.

Patients who are diagnosed with AUD should undergo a more comprehensive assessment (see [Table 12](#)) including, as appropriate and indicated, a detailed medical, mental health, and substance use history; physical examination; laboratory investigations; and risk assessment for developing severe complications of withdrawal (i.e., seizures, delirium tremens). All patients should be offered evidence-based treatment for alcohol withdrawal and



AUD (see [Withdrawal Management, Ongoing Care—Psychosocial Treatment Interventions](#), [Ongoing Care—Pharmacotherapy](#)).

### 3.3.i Diagnosis of Alcohol Use Disorder Using the DSM-5-TR

The DSM-5-TR is used to classify mental health disorders for clinical and research purposes, and it is important for clinicians to understand that heavy alcohol use alone is not sufficient to make a diagnosis of AUD.<sup>194</sup> Alcohol use disorder as defined by the DSM-5-TR is diagnosed based on patients meeting the threshold criteria of “clinically significant impairment or distress” due to their alcohol use and, among those that meet this threshold, the assessment of 11 diagnostic criteria. The severity of AUD may be mild (2–3 diagnostic criteria met), moderate (4–5 diagnostic criteria met), or severe (6 or more diagnostic criteria met).<sup>195</sup>

Alcohol abuse and dependence, which had previously been two separate diagnoses in the DSM-III and DSM-IV, are no longer diagnoses using the DSM-5-TR criteria and have been incorporated into the category of AUD. In addition to changing the classifications of AUD severity, the DSM-5-TR introduced a new criterion related to craving for alcohol and removed the criterion for recurrent alcohol-related legal problems.<sup>196</sup> Negative consequences appear to have limited ability to diagnose and define substance use disorders due to a variety of conceptual and measurement problems.<sup>197</sup>

A 2015 systematic review of diagnostic accuracy studies (N = 8, n = 68,228) found moderate to excellent agreement between the DSM-IV and DSM-5-TR (kappa = 0.60 to 0.90) criteria, with a single study reporting only moderate agreement. Further analysis of diagnostic stability indicated that between 51.4% and 92.7% of participants had both DSM-IV and DSM-5-TR AUD diagnoses across studies. Compared to the DSM-IV, the use of the DSM-5-TR criteria resulted in an increased prevalence of AUD diagnoses, particularly in non-clinical settings (e.g., general population, university students). The increased prevalence of AUD may, in part, be explained by the DSM-5-TR criteria capturing a proportion of DSM-IV “diagnostic orphans” (i.e., individuals who meet only one or two criteria for alcohol dependence and none for alcohol abuse).<sup>196</sup>

It is important to be aware of the risks of false positive diagnoses with the DSM-5-TR criteria.<sup>198,199</sup> Those who previously met criteria for alcohol abuse in the DSM-IV may now be classified as having mild to moderate AUD with the merging of diagnostic criteria for alcohol dependence and alcohol abuse. Clinicians should take care to distinguish between severe AUD, which is synonymous with the traditional definition of addiction,<sup>200</sup> and mild to moderate AUD, which may reflect harmful use but is inconsistent with the traditional definition of addiction.<sup>198,199</sup> Assessing the severity of AUD helps determine the most appropriate clinical pathway for the patient (see [Figure 1](#). Screening, Diagnosis, and Referral to Treatment Pathway).

It may be challenging to use the DSM-5-TR criteria for AUD to diagnose older adults with AUD.<sup>140</sup> There may be diagnostic uncertainty between high-risk alcohol use and mild AUD, and older adults who would otherwise meet DSM-5-TR criteria may not due to potentially reduced occupational or social obligations unrelated to alcohol use (e.g., retirement) with which alcohol might interfere.<sup>140</sup> A comprehensive assessment is indicated for all older adults who have an AUD, have signs of harmful use, or who present with acute intoxication. A comprehensive assessment should include use of a standardized alcohol use questionnaire; medication review for potential interactions; assessment of other substance use or substance use disorders; evaluation of physical, mental, and cognitive capacity, nutrition, chronic pain, social conditions, family/social supports, and overall functioning; and collateral history. The assessment should be performed regardless of physical, mental, or cognitive co-morbidities with modifications as deemed appropriate.<sup>140</sup>

Similarly for youth, it can be difficult to differentiate high-risk alcohol use from mild AUD and diagnosis using the DSM-5-TR may be prone to false positives in this context. Furthermore, very few youth in primary care meet the DSM-5-TR criteria for moderate to severe AUD. Using interview questions that further qualify the DSM-5-TR criteria for patients can help avoid false positives (see [Table 11](#) for sample clinical interview questions).

### **3.3.ii Section Summary and Recommendation**

Based on available evidence and the need to diagnose AUD to access ongoing AUD care, this guideline recommends clinicians assess patients who screen positive for high-risk drinking with a structured interview carefully applying the DSM-5-TR criteria. Patients

who are diagnosed with AUD should undergo a more comprehensive medical assessment (see [Assessment Checklist](#)) and be offered AUD care as required (i.e., withdrawal management or ongoing care). For individuals who have AUD, brief intervention may be helpful in facilitating referrals and developing a treatment plan.

Clinicians should be aware of the risks of false positive diagnoses with the DSM-5-TR. Generally, only severe AUD is consistent with the inability to stop in the face of health and social harms, consistent with the traditional definition of addiction. Careful adherence to the DSM-5-TR guide, including using qualifying interview questions, may help reduce false positive responses to the 11 criteria.

The DSM-5-TR AUD criteria appear to result in an increased prevalence of AUD diagnoses relative to the DSM-IV,<sup>196</sup> and certain populations (e.g., older adults, youth) may not be accurately identified using the DSM-5-TR criteria, while other individuals may be misclassified as having AUD if the DSM-5-TR criteria are not applied properly.

### Recommendation 3

**All adult and youth patients who screen positive for high-risk alcohol use should undergo a diagnostic interview for AUD using the DSM-5-TR criteria and further assessment to inform a treatment plan if indicated.**

LOW Quality of Evidence

STRONG Recommendation

#### Remarks

- Clinicians should diagnose and assess the severity of AUD using the DSM-5-TR criteria for AUD to help determine the most appropriate clinical pathway for the patient.
- Confirmation of diagnosis and AUD severity is crucial in connecting patients to appropriate AUD care, including offering prescriptions and providing referrals for ongoing care, where appropriate
- The DSM-5-TR criteria may not accurately identify youth or older adults with AUD who are susceptible to false positive diagnoses.
- The quality of evidence for this recommendation was rated as low based on working group consensus.
- The strength of this recommendation was rated as strong based on the quality of evidence, working group consensus, and the recognized need for diagnosis and grading of severity to enable patients to access further AUD care.

## 3.4 Brief Intervention for High-Risk Drinking

### 3.4.i Theory and Practice

Identification of patients who are drinking at high risk through screening provides the opportunity for clinicians to conduct a brief intervention (BI) to support behavioural change to reduce or discontinue alcohol consumption. Brief intervention approaches can vary in a number of components, such as the duration and number of clinician–patient interactions involved, and many incorporate principles of motivational interviewing (MI), an evidence-based counselling approach. Clinicians should be aware that BI alone may not be sufficient support for all patients to meet their goals around alcohol use, and some patients may need to engage in other interventions.

Motivational interviewing is a counselling approach that helps patients enhance their motivation to change and creates a therapeutic alliance that is predominantly a partnership, rather than an expert/patient dynamic.<sup>201</sup> The general principles of MI are partnership, acceptance, compassion, and evocation.<sup>201</sup> The intended outcome of MI is to bring awareness to the patient of any discrepancies between their current behaviours and their values and future goals. MI-based counselling does not require professional specialization and can be delivered by primary care physicians, nurse practitioners, nurses, and other regulated health professionals who have completed appropriate training, although referral to specialist care should be made when appropriate.

Brief intervention approaches that adhere to the principles of MI are typically structured using the FRAMES approach,<sup>201</sup> a mnemonic device that stands for **F**eedback, **R**esponsibility, **A**dvice, **M**enu, **E**mpathic, and **S**elf-efficacy (see [Table 13](#)).<sup>201,202</sup> An example that has been well studied in primary care is the “5A’s” model for behavioural change.<sup>203</sup> The 5A’s model was originally developed to facilitate the adoption of universal screening and brief intervention for tobacco cessation, but has been adapted for a number of other health behaviours, including alcohol use.<sup>106,204</sup> The 5A’s stand for **A**sk, **A**dvice, **A**ssess, **A**ssist, and **A**rrange (see [The 5A’s Model for Brief Alcohol Interventions](#)). Ease of recall and brevity are practice-relevant strengths of this approach. The 5A’s can also be easily adapted to specific

clinical settings and patient populations (e.g., question order and format can be modified as needed), and other members of the primary care team can administer the 5A's if prescriber time is limited.

**Key aspects of BI include discussing the patient's health concerns, collaboratively setting goals, and developing a treatment plan tailored to those goals and patient preferences.**

Patients who are pre-contemplative or ambivalent about reducing their alcohol consumption can be reassessed at subsequent appointments to determine whether their alcohol consumption and related circumstances have changed. Detailed guidance on delivering BI can be found in [Appendix 3: Brief Intervention for High-Risk Alcohol Use and AUD](#).

### 3.4.ii Brief Intervention

There is a robust evidence base to support the use of BI for high-risk drinking in adults, youth (aged 11–25 years),<sup>166,205</sup> and university students.<sup>172,206-208</sup> Several high-quality meta-analyses and systematic reviews have demonstrated that BI results in clinically meaningful reductions in high-risk drinking behaviours, including heavy episodic drinking, high daily or weekly levels of alcohol consumption, and drinking that exceeds recommended alcohol consumption limits, and concluded that, overall, there is a moderate beneficial effect of BI.<sup>209-214</sup> For example, a 2018 Cochrane review (N = 69 RCTs, n = 33,642) reported moderate quality evidence that alcohol-related BIs administered in primary care settings led to sustained reductions in alcohol use up to one year later. On average, participants who received brief intervention consumed 1.5 fewer drinks per week (-20g, 95% CI: -11.81g to -28.36g) and reported fewer binges (mean difference (MD): -0.08; 95% CI: -0.02 to -0.14) and drinking days (MD: -0.13; 95% CI: -0.04 to -0.14) per week compared to participants who received minimal or no intervention. However, grams of alcohol consumed per drinking day were equivalent between groups.<sup>209</sup>

Although a 2012 systematic review (N = 23, n = 10,745) reported the strongest effect sizes with multi-contact brief interventions (i.e., multiple 10–15 minute BI sessions

**A single, 5-minute brief intervention session is likely to be effective in reducing alcohol consumption**

delivered over a timespan of up to 1 year),<sup>144</sup> other reviews have found that extending the duration and frequency of brief interventions does not appear to confer significant advantages.<sup>209,215</sup> A consistent finding across multiple reviews is that even a single, 5-minute session incorporating the core principles of MI is likely to be effective in reducing alcohol consumption among individuals at higher risk of alcohol-related harms.<sup>205</sup> A 2016 meta-analysis of 52 RCTs (n = 29,891) found that provider type (e.g., counsellors, peer support staff, social workers, psychologists) did not impact outcomes, with some evidence that BI delivered by nurses was more effective than physician-, counsellor- or peer-delivered BIs in reducing the quantity of alcohol consumed by individuals with high-risk drinking patterns (Cohen's *d*<sup>t</sup>: -0.23, 95% CI: -0.33 to -0.13).<sup>216</sup> Thus, if physician and nurse practitioner time is limited, delegation of screening and BI to other trained members of the care team or staff can be considered.

### 3.4.ii.1 Technology-based Brief Intervention

Use of technology-based BI (i.e., BI delivered via a web-based format, smartphone, or other technology) is increasing in primary care and community settings.

Multiple meta-analyses, systematic reviews, and RCTs suggest it may be effective in improving alcohol-related outcomes and reducing alcohol-related harms.<sup>217-228</sup>

For example, a 2019 systematic review of 42 studies (n = 19,135) found that 71% of studies reported reduced alcohol consumption or harm in all primary or secondary efficacy outcomes (i.e., quantity of alcohol use, frequency of alcohol use, severity of alcohol or risk scores, binge or heavy episodic drinking, status of at-risk alcohol use, any use, and drinking consequences) following technology-based brief intervention.<sup>217</sup> These findings align with a 2018 meta-analysis of individual patient data from 19 RCTs (n = 14,198) that demonstrated technology-based

<sup>t</sup> Cohen's *d* is a measure of effect size. A result of 0.2 is a small effect size, 0.5 is a medium effect size, and 0.8 is a large effect size.

brief intervention significantly reduced mean weekly alcohol consumption (-5.02 standard units, 95% CI: -7.57 to -2.48;  $p < .001$ ) and increased participant adherence to lower-risk drinking guidelines (OR = 2.20, 95% CI: 1.63 to 2.95;  $p < .001$ ; NNT = 4.15).<sup>218</sup> Technology-based brief interventions have potential to be scaled up; however, more research is needed to identify which populations may experience the greatest benefit and which delivery contexts best support patients.<sup>218</sup>

### 3.4.iii Brief Intervention in Youth

Multiple meta-analyses and systematic reviews have demonstrated the effectiveness of BI in improving alcohol outcomes among youth. For example, a 2020 network meta-analysis (N = 22, n = 5,668) found BI resulted in significantly fewer days of alcohol use (-1.1 days per month, 95% credible interval: -2.2 to -0.3) and days of heavy alcohol use (-0.7 days per month, 95% credible interval: -1.6 to 0.0) compared to treatment as usual for youth aged 12–20; however, there was no significant difference in abstinence rates.<sup>229</sup> Similarly to adult populations, technology-based BI may be a feasible option for youth, with evidence from a 2019 systematic review (N = 53, n = 31,365) demonstrating a small reduction in alcohol consumption at 6-months compared to no intervention (standard mean difference [SMD]: -0.18, 95% CI: -0.29 to -0.08) or assessment only (SMD: -0.14, 95% CI: -0.02 to -0.09) in youth aged 15–25.<sup>219</sup> Both indicated and universal (i.e., preventive) BI have been found to result in clinically important outcomes for alcohol use and related indices in youth aged 12–18.<sup>230</sup> However, there is a lack of research on best practices for delivery, communication methods, and intervention-specific components that could influence “real-world” effectiveness of BI in this population.<sup>230</sup>

Primary care providers are well-positioned to offer BI to youth and youth may be more likely to participate in BI offered in a primary care setting compared to a specialist setting. In a 2020 study that randomized 7 primary care clinic sites to implement a generalist-led or specialist-led screening, brief intervention, and referral to treatment (SBIRT) model using the CRAFFT as the screening tool, 24.4% of adolescents (aged 12–17) in the specialist-led model declined an appointment with a specialist to receive BI following screening, while only 3.8% of adolescents declined BI provided by their primary care provider in the generalist-

led model, suggesting that the specialist-led SBIRT model was less effectively implemented.<sup>231</sup> The lower rate of administered BI in the specialist-led SBIRT model may reflect the patient's willingness to continue a conversation about their substance use with a possibly new and unfamiliar care provider.

In the Canadian context, key messages for youth that could be adapted into BI are to encourage youth to delay drinking until they are of legal age ( $\geq 18$  or 19 years of age).<sup>232,233</sup> If youth decide to drink, strategies for reducing harm can be discussed, such as ensuring that drinking occurs in a safe environment and limiting alcohol consumption to 1–2 drinks at a time, 1–2 times per week.<sup>232,233</sup> Youth may also benefit from youth-specific spaces for substance use and mental health services and clinicians are encouraged to provide information to youth on what is available in their community. Further guidance can be found in [Appendix 3: Brief Intervention for High-Risk Alcohol Use and AUD](#).

#### **3.4.iv Brief Intervention in Pregnant Patients**

A 2009 systematic review (N = 4, n = 715) of randomized clinical trials examining the effectiveness of psychosocial interventions found that BI may motivate pregnant patients to reduce or discontinue alcohol use; however, due to insufficient and heterogeneous data, a meta-analysis could not be performed.<sup>234</sup> A number of individual studies have reported significant results in favour of BI in this population. For example, a 2007 randomized trial (n = 255) that compared BI to assessment only found that pregnant individuals who received a BI were five times more likely to discontinue alcohol use throughout their pregnancy than those who received assessment only (OR: 5.29, 95% CI: 1.59 to 18.25).<sup>235</sup> Perinatal outcomes were also improved in the BI group: infant mortality rate was three times lower (0.9% versus 2.9%) and infants had clinically significant greater birth length ( $p = .03$ ) and weight ( $p = .06$ ) in the BI group than the assessment-only group.<sup>235</sup>

As with the general patient population, the most frequently studied form of BI in this population is MI, including the 5A's model.<sup>185,236,237</sup> However, research has also shown that simply asking pregnant patients about their alcohol use, discussing potential risks, and offering brief, non-judgmental advice may help modify drinking behaviour.<sup>185,238</sup>



### 3.4.v Brief Intervention in Older Adults

A 2014 systematic review (N = 37) of brief interventions for the general adult population noted that there is a lack of literature regarding the use of brief interventions for older adults.<sup>205</sup> A subsequent systematic review (N = 7, n = 3,531) revealed an overall positive effect on alcohol-related outcomes (e.g., alcohol consumption, drinks per week, heavy drinking days) following brief intervention; however, the authors emphasize the need for further research specific to older adults.<sup>239</sup> The CCSMH's [Canadian Guidelines on Alcohol Use Disorder Among Older Adults](#) suggest that brief intervention should be explored initially with older adults who have mild AUD, as it is the least intrusive treatment option.<sup>140</sup> A 2022 systematic review (N = 61<sup>u</sup>, n = 51,360) identified three major effective elements of interventions that contribute to the prevention or reduction of alcohol use in older adults (aged 55+): providing information on the consequences of alcohol consumption, providing individualized feedback on alcohol use based on their age and other factors, and the patient having contact with others and communicating with them about alcohol use.<sup>240</sup> Brief intervention provides an opportunity to incorporate all three of these elements.

### 3.4.vi Section Summary and Recommendation

Based on available evidence, this guideline recommends that clinicians offer BI to all adult and youth patients who screen positive for high-risk alcohol use. Several high-quality systematic reviews have found that BI results in significant and clinically meaningful reductions in alcohol consumption, and have concluded that, overall, there is moderate-quality evidence for the beneficial effect of BI.<sup>26,157,209,241</sup>

The committee endorses the use of short, practice-friendly motivational interviewing-based approaches in a manner aligned with the [Principles of Care](#)

- 
- u The vast majority of studies included in this systematic review were not focused on older adults. Instead, interventions were more commonly targeted at the general population and inclusive of individuals aged 55 years or older.

to support behavioural change such as the 5A's model, as these approaches have been well-studied and are likely familiar to many primary care providers.<sup>106,204</sup>

Involving interprofessional staff or teams in the screening and brief intervention pathway is recommended if clinician time is limited and to ensure that all patients are screened and triaged appropriately. Research has shown that BI delivered by counsellors, peer support staff, social workers, or psychologists is as effective as physician-delivered BI in supporting patients to reduce drinking and alcohol-related harms, and interventions delivered by nurses may be more effective than physician-delivered BI.<sup>216</sup>

## Recommendation 4

**All patients who screen positive for high-risk alcohol use should be offered brief intervention.**

**MODERATE** Quality of Evidence

**STRONG** Recommendation

### Remarks

- Clinicians should have access to appropriate training, education, and resources for delivering BI.
- Brief intervention and continued monitoring should be offered to patients who screen positive for high-risk drinking. For those diagnosed with AUD, BI should be offered along with appropriate psychosocial and/or pharmacological interventions.
- The quality of evidence for this recommendation was rated as moderate based on systematic reviews that found BI resulted in significant and clinically meaningful reductions in high-risk drinking behaviours, including heavy episodic drinking, high daily or weekly levels of alcohol consumption, and drinking that exceeds recommended alcohol consumption limits.
- The strength of this recommendation was rated as strong based on quality of evidence, working group consensus, cost-effectiveness, and the effectiveness of BI.

## 3.5 Implementing Screening and Brief Intervention in Practice

Implementation of universal screening and BI for alcohol use has been recommended by a range of national and international organizations, including the Canadian National Alcohol Strategy Working Group, the Canadian Task Force on Preventive Health Care, the Canadian Paediatric Society, the US Preventive Services Task Force, the American Academy of Pediatrics, and the World Health Organization.<sup>145,202,242-246</sup> However, implementation of universal alcohol screening and brief intervention in clinical practice has proven challenging, with reported rates of uptake as low as 2% for alcohol use screening and 1% for BI.<sup>247</sup> Barriers most often cited by primary care providers include a lack of time, education, training, and resources; personal discomfort and unease around how to communicate with patients; stigma manifesting in beliefs that patients will not change their behaviour; and fear of offending patients with questions about alcohol consumption.<sup>248</sup>

These barriers may also underpin discrepancies between efficacy and effectiveness studies. Despite randomized trials that demonstrate the efficacy of BI in research settings, a number of recent trials report modest or no differences in alcohol consumption following widespread implementation of universal alcohol use screening and BI in private and publicly-funded care systems.<sup>249-252</sup> In these studies, the authors specifically cited low rates of provider compliance in administering BI as per study protocols as a contributing factor. Organizational or system-level factors, such as provider incentives, educating providers about the risks of alcohol use and effectiveness of BI, addressing stigma, and providing training for delegated staff (e.g., nurses, regulated health professionals) could facilitate wider implementation and improve effectiveness in the primary care context.<sup>248-252</sup>

In the United States, funding for SBIRT initiatives for substance use have been prioritized by the National Institutes of Health for over a decade, and robust evaluations of large-scale implementation projects are available.<sup>253-257</sup> Through

this work, a number of similar themes have emerged among successful programs. These best practices for successful uptake and implementation of substance use SBIRT are summarized below.

*Box 4. Best Practices for Implementing SBIRT in Primary Care Settings*<sup>253-257</sup>

- Identify a “practice champion” or champions
- Ensure buy-in from leadership and senior staff
- Involve all members of the care team and clinic staff
- Clearly define and communicate each step of the SBIRT pathway to all team members
- Develop functional referral pathways with external partners and programs
- Institute ongoing and regular opportunities for staff training/re-training in SBIRT
- Align the SBIRT pathway within the primary care clinic flow such that disruptions are minimal and change is readily adopted
- Use a brief, validated screening instrument (e.g., SASQ) prior to a full screen
- Integrate SBIRT into the electronic health record
- Use computerized reminders to prompt actions in the SBIRT pathway
- Implement performance measures

# 4 Withdrawal Management

Withdrawal management is defined as a set of pharmacological, psychosocial, and supportive care interventions that aim to manage withdrawal symptoms or withdrawal syndrome that occur when an individual with a substance use disorder ceases or significantly reduces consumption of that substance.<sup>258</sup> Comprehensive withdrawal management provides care to patients as they withdraw from a substance (i.e., detoxification) as well as supporting the patient to stabilize, connect to ongoing care, and access other health and social services.<sup>259</sup> Withdrawal management is also a critical time to refer individuals to ongoing supports. Importantly, for individuals with moderate or severe AUD, medically supervised withdrawal management can prevent potentially life-threatening complications that can emerge if the patient is left untreated (i.e., seizures, delirium tremens).<sup>258</sup> For this reason, it is critical to distinguish between individuals at risk of severe withdrawal complications from individuals with mild to moderate withdrawal symptoms.

Research has shown that completion of withdrawal management prior to starting AUD pharmacotherapy can improve treatment outcomes by preventing early return to drinking (or relapse), which is often associated with untreated withdrawal symptoms.<sup>260-262</sup> Completion of withdrawal management may also be required prior to admission to bed-based treatment (previously called residential treatment programs) and other support or recovery programs that require abstinence and do not support medicalized withdrawal.

Withdrawal management may be necessary or recommended for patients for numerous reasons. Withdrawal management can reduce the risk of experiencing severe withdrawal symptoms, help to prevent return to drinking, and support patient goals (e.g., managing mild to moderate withdrawal symptoms, linking patients to ongoing care). All patients should be assessed based on their risk of developing severe complications from withdrawal (i.e., seizures, delirium tremens) and other clinical considerations for stratification into withdrawal management pathways. Risk levels can be assessed using the Prediction of Alcohol Withdrawal Severity Scale (PAWSS)<sup>263</sup> alongside consideration of patient circumstances and preference. Patients assessed to be at high risk of developing severe complications (i.e., seizures, delirium tremens) should be referred to an inpatient facility to receive treatment under a level of clinical observation appropriate to the patient's

risk level. Patients at low risk of developing severe complications may not require inpatient withdrawal management and withdrawal can be safely treated through home-based withdrawal management programs, specialized outpatient addiction services, and primary care settings. Clinicians may determine that it is most appropriate for a patient to be referred to inpatient withdrawal management or an individual may express a preference for inpatient withdrawal management, regardless of PAWSS score. Some patients may also begin AUD ongoing care pharmacotherapy or psychosocial treatment interventions immediately (see [Ongoing Care—Pharmacotherapy](#) and [Ongoing Care—Psychosocial Treatment Interventions](#)).<sup>264</sup> Clinicians should be aware, however, that most AUD ongoing care pharmacotherapies do not address withdrawal symptoms, no ongoing care pharmacotherapy has been shown to prevent severe complications of withdrawal, and that alcohol withdrawal symptoms can still occur in individuals at low risk of severe withdrawal due to a sudden or significant reduction in alcohol consumption. Clinicians should closely monitor these patients during early stages of treatment.

Withdrawal management alone is a short-term intervention that can be life-saving and it is recommended that all patients be offered a referral to ongoing care following completion of withdrawal management. Based on patient goals and available resources, withdrawal management should ideally lead to engagement in ongoing pharmacotherapy, psychosocial care, or both. In circumstances in which withdrawal management alone is the only available in-person treatment (e.g., in rural and remote or under-resourced settings), clinicians should offer withdrawal management and a referral to virtual ongoing care (e.g., virtual appointments to prescribe pharmacotherapy and to provide or refer to psychosocial treatment, including peer support groups).

## 4.1 Overview of Alcohol Withdrawal

Alcohol primarily affects the central nervous system (CNS) by acting as a *gamma*-aminobutyric acid (GABA) agonist and glutamate antagonist. Normally, the brain maintains a balance between the inhibitory effects of GABA and excitatory effects of glutamate. Alcohol disrupts this balance by increasing the inhibitory effects of GABA and suppressing the excitatory effects of glutamate, resulting in calm or relaxed feelings, reduced inhibitions, impaired balance and coordination, and slowed reaction speed, cognition, and breathing rate.<sup>265</sup> With chronic alcohol

use, the brain adapts and compensates for its effects; GABA-mediated systems become less sensitive to GABA and glutamate-mediated systems become more sensitive to glutamate to restore neurochemical equilibrium.<sup>266</sup> In these conditions, a sudden cessation or a significant reduction of alcohol consumption triggers an acute imbalance between the GABA and glutamate systems, resulting in an overall state of CNS excitation and a lower seizure threshold.<sup>266</sup> This mechanism explains many symptoms of alcohol withdrawal that occur in patients with a history of chronic heavy alcohol use when they abruptly discontinue or significantly reduce alcohol intake.

Up to 50% of individuals with long-term AUD will experience some degree of withdrawal upon cessation of alcohol use.<sup>267-269</sup> Symptoms of alcohol withdrawal typically begin 6–24 hours after the last intake of alcohol and reach peak intensity at 24–48 hours, with resolution of most symptoms within 5–7 days.<sup>270</sup> Within hours of alcohol use cessation, autonomic hyperactivity can present as tachycardia, pyrexia, tremor, nausea, vomiting, and sweating, which may also be accompanied by psychological distress in the form of anxiety, restlessness, and sleep disturbance or insomnia (see [Box 5](#)).

Data on the natural history of alcohol withdrawal has mainly been derived from studies of medically ill, hospitalized patients. These studies have shown that, while alcohol withdrawal is typically limited to the symptoms listed above, approximately 7–8% of symptomatic individuals may also experience transient visual, auditory, or tactile hallucinations.<sup>271</sup> Additionally, approximately 10% of symptomatic patients experience withdrawal-related generalized tonic-clonic seizures that require medical intervention.<sup>264,272</sup> If left untreated, approximately one-third of individuals experiencing withdrawal seizures are at risk of progression to delirium tremens.<sup>273</sup> Delirium tremens is the most serious manifestation of alcohol withdrawal and is characterized by the onset of severe confusion, disorientation, or hallucinations accompanied by severe autonomic hyperactivity.<sup>274</sup> Delirium tremens occurs in approximately 3–5% of patients who are hospitalized for the management of alcohol withdrawal<sup>265,267,275</sup> and if left untreated, the risk of death is approximately 3–5%.<sup>276</sup> Patients may experience common and less severe symptoms, such as shakes and tremors, and confuse them with more severe symptoms, specifically seizures and delirium tremens. During diagnosis, clinicians should clearly define withdrawal symptoms and ensure patient understanding of each symptom prior to eliciting the patient's response.

### Box 5. DSM-5-TR Diagnostic Criteria for Alcohol Withdrawal Syndrome<sup>3</sup>

A. Cessation of (or reduction in) alcohol use that has been heavy and prolonged.
B. Two (or more) of the following, developing within several hours to a few days after the cessation of (or reduction in) alcohol use described in Criterion A: <ol style="list-style-type: none"><li>1. Autonomic hyperactivity (e.g., sweating or pulse rate greater than 100bpm).</li><li>2. Increased hand tremor.</li><li>3. Insomnia.</li><li>4. Nausea or vomiting.</li><li>5. Transient visual, tactile, or auditory hallucinations or illusions.</li><li>6. Psychomotor agitation.</li><li>7. Anxiety.</li><li>8. Generalized tonic-clonic seizures.</li></ol>
C. The signs or symptoms in Criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
D. The signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication or withdrawal from another substance.

Specify if:

- **With perceptual disturbances:** This specifier applies in the rare instance when hallucinations (usually visual or tactile) occur with intact reality testing, or auditory, visual, or tactile illusions occur in the absence of a delirium.

**Coding note:** The ICD-10-CM code depends on whether or not there is a comorbid alcohol use disorder and whether or not there are perceptual disturbances.

- **For alcohol withdrawal, without perceptual disturbances:** If a mild alcohol use disorder is comorbid, the ICD-10-CM code is **F10.130**, and if a moderate or severe alcohol use disorder is comorbid, the ICD-10-CM code is **F10.230**. If there is no comorbid alcohol use disorder, then the ICD-10-CM code is **F10.930**.
- **For alcohol withdrawal, with perceptual disturbances:** If a mild alcohol use disorder is comorbid, the ICD-10-CM code is **F10.132**, and if a moderate or severe alcohol use disorder is comorbid, the ICD-10-CM code is **F10.232**. If there is no comorbid alcohol use disorder, then the ICD-10-CM code is **F10.932**.

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## 4.2 Assessment of Withdrawal Symptoms at Point-of-Care

Periodic measurement of symptoms during withdrawal from alcohol has been shown to facilitate appropriate adjustments in dosing and mitigate the risk of severe symptoms, as high scores early in the course of treatment are predictive of severe withdrawal complications, including seizures and delirium.<sup>277-279</sup> Several alcohol withdrawal symptom severity assessment scales have been published; of these, the Clinical Institute Withdrawal Assessment—Alcohol Revised (CIWA-Ar) and the Short Alcohol Withdrawal Scale (SAWS) are the two most widely used and recommended tools for measuring withdrawal symptoms.<sup>279-281</sup>

### 4.2.i The Clinical Institute Withdrawal Assessment—Alcohol Revised

The CIWA-Ar is the most widely used tool<sup>282</sup> for assessing withdrawal symptom severity in a range of clinical care settings, with demonstrated inter-rater reliability and validity.<sup>283</sup> The CIWA-Ar involves clinician assessment of 10 individual symptoms and signs of alcohol withdrawal, including anxiety and agitation; auditory, visual, and tactile disturbances; tremor; sweating; nausea; headache; and clouding of sensorium, which are assigned a numerical score based on objective and subjective measures of severity (see [Box 14](#)).<sup>283</sup> The CIWA-Ar is not suitable for self-assessment and should be administered by a clinician.

The CIWA-Ar can be used to determine medication dosing schedules prior to treatment initiation and periodically during withdrawal management (i.e., symptom-triggered schedules). Studies have shown that using the CIWA-Ar in this context minimizes both under- and over-medicating patients.<sup>279,280</sup>

Use of the CIWA-Ar may not be appropriate if there are any barriers to communication between provider and patient (e.g., language, verbal capacity, cognitive impairments, or decreased level of consciousness), or if the patient shows signs of instability, disorientation, or delirium. Clinicians should be aware that such circumstances may undermine the validity of scores for subjective CIWA-Ar items symptoms that require discussion with the patient to accurately assess (e.g., anxiety, headache, nausea, hallucinations).<sup>284</sup> The CIWA-Ar has

not been validated in patients using alcohol along with other CNS depressants (e.g., opioids, benzodiazepines) and there is a risk for opioid or benzodiazepine withdrawal to be misidentified as symptoms of alcohol withdrawal.<sup>279,280</sup>

#### 4.2.ii Short Alcohol Withdrawal Scale

The SAWS was developed with a focus on minimizing length, observer bias, and communication barriers that can hinder the objective scoring of alcohol withdrawal symptoms.<sup>285,286</sup> Similar to the CIWA-Ar, the SAWS scoring tool consists of 10 symptoms, with the severity of each symptom assigned a score from non-existent (0) to severe (3) (see [Box 15](#)). Patients reporting a combined score of 12 or higher are considered to be candidates for pharmacological withdrawal management.<sup>285</sup> Scoring the SAWS takes 5–10 minutes and can be completed either by the patient or in a structured interview format in inpatient or outpatient settings.<sup>285</sup>

Cited advantages of the SAWS instrument are its brevity and ease of interpretation and use by patients and clinicians alike.<sup>285,286</sup> A 2010 randomized study involving 122 patients validated the use of the SAWS in outpatient settings and found that SAWS was easy to understand and relevant to treatment selection and evaluation.<sup>286</sup> Additionally, it is suggested that completion of the SAWS by patients may help eliminate observation bias and remove practical barriers imposed by frequent scoring among clinical staff.<sup>286</sup> As such, the SAWS may serve as a standalone tool for assessing mild to moderate alcohol withdrawal symptoms or a supplement to clinician-administered tools such as CIWA-Ar. Similar to the CIWA-Ar, the use of the SAWS is limited if there are any barriers to communication or comprehension (e.g., language, low literacy).<sup>286</sup>

### 4.3 Assessing Risk of Severe Complications of Alcohol Withdrawal

Not all individuals with AUD will experience severe complications upon reduction or cessation of alcohol use; for example, some reviews suggest that youth, those who consume less alcohol, and individuals with a shorter lifetime history or severity of AUD may be less likely to experience severe complications.<sup>267-269</sup>

A widely cited theory known as the “kindling effect”<sup>287</sup> suggests that the severity of withdrawal symptoms experienced by a patient directly correlates to their alcohol use history (e.g., duration of any alcohol use and duration of heavy alcohol use) and previous experiences of withdrawal (e.g., number of previous attempts at abstinence, symptom severity, history of complications). The kindling theory proposes that repeated episodes of untreated alcohol withdrawal symptoms progressively increase neural excitability and may lower the seizure threshold. This can lead to successively more severe withdrawal episodes that have an increased likelihood of progression to seizures and delirium tremens.<sup>273,288</sup>

A systematic method for predicting the risk of severe withdrawal symptoms based on alcohol use history, withdrawal history, and other relevant factors can help to inform decision-making when selecting withdrawal management pathways and devising tailored strategies for individual patients.<sup>v</sup> Identifying patients at low risk of severe complications can help to reduce unnecessary acute care admissions and medication use. This also potentially allows for the use of a non-benzodiazepine or benzodiazepine-sparing approach, which can reduce adverse effects commonly observed with benzodiazepines, such as over-sedation, falls, delirium, memory impairment, respiratory depression, coma, dependence, and prolonged hospitalization.<sup>289,290</sup>

### 4.3.i The Prediction of Alcohol Withdrawal Severity Scale

The Prediction of Alcohol Withdrawal Severity Scale (PAWSS) is a validated score-based tool for estimating the risk of severe withdrawal which can inform the selection of appropriate withdrawal management pathways (see [Box 16](#) for the tool).<sup>263</sup>

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- v Some individuals who drink heavily may be at risk of developing withdrawal symptoms without meeting the diagnostic criteria of AUD. Clinicians should initiate withdrawal management when it is medically necessary, regardless of AUD diagnosis.

*Box 6. Predictive factors for severe alcohol withdrawal and complications*<sup>263,268,274</sup>

- Previous episodes of alcohol withdrawal, seizures, delirium tremens, inpatient alcohol rehabilitation treatment, or blackouts
- Co-occurring use of CNS-depressant agents (e.g., opioids, benzodiazepines, barbiturates) or other licit or illicit substances
- Recent intoxication; positive blood alcohol level on admission to care
- Evidence of increased autonomic activity, including elevated blood pressure, heart rate, and body temperature

The PAWSS incorporates the risk factors listed above into a 10-item cumulative scale with a maximum score of 10, wherein a score < 4 indicates low risk and a score ≥ 4 indicates high risk for severe complications of withdrawal.<sup>263</sup>

A 12-month prospective study of 403 hospitalized patients published in 2015 showed that the PAWSS had a high predictive value for identification of patients at high-risk of severe complications (positive predictive value [PPV]<sup>w</sup> = 93.1; negative predictive value [NPV]<sup>x</sup> = 99.5) and good inter-rater reliability (96.3% agreement).<sup>291</sup> The authors concluded that this tool may enable clinicians to accurately identify patients at risk of severe complications and devise an appropriate treatment plan to prevent these symptoms.<sup>291</sup>

The accuracy and usefulness of the PAWSS was further demonstrated in a 2018 meta-analysis of 14 studies (n = 71,295) evaluating single and composite measures of severe withdrawal risk.<sup>292</sup> The authors demonstrated that, while no single factor could be used to exclude the risk of severe withdrawal management syndrome, a history of delirium tremens (likelihood ratio [LR]<sup>y</sup> = 2.9, 95% CI: 1.7

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w Positive predictive value reflects the proportion of subjects with a positive test result who truly have the outcome of interest.

x Negative predictive value reflects the proportion of subjects with a negative test result who truly do not have the outcome of interest.

y The likelihood ratio (LR) gives the probability of correctly predicting disease in ratio to the probability of incorrectly predicting disease. An LR > 1 indicates that the test increased the assessment of the disease probability; LR < 1, it decreased. An LR of 1 indicates that no diagnostic information is added by the test.

to 5.2) and baseline systolic blood pressure of 140mmHg or higher (LR = 1.7, 95% CI: 1.3 to 2.3) were associated with an increased likelihood of developing severe complications of alcohol withdrawal. The review also demonstrated that composite scales (i.e., PAWSS, Luebeck Alcohol Withdrawal Risk Scale,<sup>293</sup> and Alcohol Withdrawal Rating Scale<sup>294</sup>) that measured multiple signs and symptoms were more useful in predicting an individual's risk than individual signs or symptoms. Of these composite scales, the PAWSS was found to be the most accurate, with a positive LR of 174 (95% CI: 43 to 696; specificity = 0.93) and a negative LR of 0.07 (95% CI: 0.02 to 0.26; sensitivity = 0.99).<sup>292</sup>

As noted in the 2018 meta-analysis,<sup>292</sup> the PAWSS has not yet been validated in outpatient care settings, youth, or pregnant individuals. It should also be emphasized that this tool is not suitable for self-assessment; the administering clinician should clearly define the criteria in the PAWSS questionnaire for the patient in order to minimize the risk of a false positive result.

**As with any other assessment tool, the PAWSS is intended for use in conjunction with clinical information, clinical resources, and patient preference. The biggest risk factor for severe withdrawal complications is a history of past severe withdrawal including past seizures or delirium tremens.<sup>295,296</sup> Due to the severity of these outcomes, clinicians should consider past history, client circumstances (e.g., unsafe housing, homelessness, intimate partner violence; see [Box 7](#)), and clinical resources for best matching patients with the appropriate level of care.**

All patients diagnosed with AUD should be assessed for the risk of developing severe complications of alcohol withdrawal, even if a patient opts not to start treatment or if withdrawal management is not part of a patient's treatment plan. Severe complications can occur with sudden or significant reductions in or discontinuation of alcohol use. Clinicians should review PAWSS scores with patients and provide education on the risks associated with unsupervised withdrawal.

The PAWSS can only be used to predict the risk of severe complications of withdrawal. Actively occurring withdrawal symptoms can be assessed with the CIWA-Ar scale or the SAWS.

### 4.3.ii Section Summary and Recommendation

The guideline committee recommends the use of the PAWSS to assess risk of severe complications of alcohol withdrawal and to help inform the stratification of patients to outpatient (e.g., PAWSS < 4) or inpatient (e.g., PAWSS ≥ 4) withdrawal management care pathways. This recommendation is based on the results of a prospective study that found the PAWSS had an excellent predictive value (PPV = 93.1; NPV = 99.5) for identification of patients at risk of severe complications<sup>291</sup> and a 2018 meta-analysis that found that the PAWSS had the highest sensitivity (93%) and specificity (99%) for identifying patients at risk of severe alcohol withdrawal compared to other composite scales (i.e., Luebeck Alcohol Risk Scale and Alcohol Withdrawal Rating Scale) and compared to individual signs and symptoms.<sup>292</sup>

## Recommendation 5

**Clinicians should use clinical parameters, such as past seizures or past delirium tremens, and the Prediction of Alcohol Withdrawal Severity Scale (PAWSS) to assess the risk of severe alcohol withdrawal complications and determine an appropriate withdrawal management pathway.**

MODERATE Quality of Evidence

STRONG Recommendation

### Remarks

- This tool should be used in conjunction with a comprehensive assessment of a patient's medical history, current circumstances, needs, and preferences.
- The PAWSS is not suitable for self-assessment and should be administered by a clinician.
- Patients may confuse some of the criteria included in the PAWSS questionnaire, specifically seizures and delirium tremens, with common and less severe symptoms of withdrawal. To avoid false positives, the administering clinician should clearly define these criteria prior to obtaining the patient's responses.
- The PAWSS has not been validated in outpatient care settings, pregnant individuals, or youth populations.
- The quality of evidence for this recommendation was rated as moderate because the PAWSS has demonstrated strong accuracy in a small number of prospective studies in limited populations.
- The strength of this recommendation was rated as strong based on the quality of evidence, working group consensus, cost-effectiveness, feasibility of implementing PAWSS in clinical settings, and the usefulness of risk stratification to inform patient care pathways.

## 4.4 Withdrawal Management Strategies

This section reviews criteria for outpatient and inpatient withdrawal management strategies. Clinicians should use the PAWSS, alongside other patient criteria, to assess for the risk of severe complications from alcohol withdrawal and to inform the selection of the appropriate withdrawal management pathway. Patients at low risk of severe complications of alcohol withdrawal (e.g., PAWSS < 4) generally can undergo withdrawal management in an outpatient setting, while patients at high risk of severe withdrawal complications (e.g., PAWSS ≥ 4) should generally be referred to inpatient withdrawal management where available.

### 4.4.i Outpatient Withdrawal Management

It is estimated that up to 80% of patients with AUD can undergo medically supervised withdrawal management in an outpatient care setting (e.g., primary care offices, addiction treatment facilities).<sup>297,298</sup> Outpatient management is generally safe, effective, and more cost-effective than inpatient treatment<sup>298,299</sup> and may be less disruptive to a patient's work and family life.<sup>300</sup> Moreover, reviews report that more than 70% of patients enrolled in outpatient withdrawal management complete treatment and 50% of these patients remain engaged in ongoing addiction care to meet long-term treatment goals (i.e., a reduction in heavy drinking or alcohol related harms, or abstinence).<sup>295,301</sup> Specific patient criteria for outpatient withdrawal management are listed below.

## Box 7. Patient Criteria for Outpatient Alcohol Withdrawal Management<sup>295,296</sup>

All of the following criteria should be met:

- PAWSS score < 4 (see [Box 16](#))
- Absence of contraindications and conditions that could indicate inpatient withdrawal management regardless of PAWSS score:
  - Multiple unsuccessful attempts at outpatient withdrawal management
  - History of seizures or delirium tremens
  - Severe or uncontrolled comorbid medical conditions (e.g., severe or uncontrolled diabetes, COPD, heart disease)
  - Severe liver compromise (e.g., jaundice, ascites, decompensated cirrhosis)
  - Acute confusion or cognitive impairment
  - Acute illness or infection requiring medical intervention
  - Concurrent serious psychiatric symptoms or unstable psychiatric disorders (e.g., suicidal ideation, psychosis)
  - Withdrawal management for more than one substance or stabilization on more than one pharmacotherapy treatment for substance use
  - Concurrent use of other CNS depressants (e.g., prescribed or non-medical use of Z-drugs, benzodiazepines, barbiturates, opioids)
  - Chronic, complex pain disorders
  - Pregnancy
  - Lack of a safe, stable, and substance-free setting (e.g., experiencing homelessness) or reliable person (e.g., family member, friend, caregiver, pharmacist, community support person) to dispense medication
  - Lack of adequate response to non-benzodiazepine medications after 24–48 hours
- Ability to follow up for the first 3–5 days and alternating days thereafter
  - If in-person visits are not feasible for patients or clinicians, virtual follow-up options such as phone or video calls should be offered
- Ability to take oral medications
- Ability to understand medical instructions
- Safe housing (i.e., housing that does not jeopardize the health, safety, or welfare of its occupant(s) and provides access to basic utilities).
- Has a reliable person (e.g., family member, friend, caregiver, pharmacist, community support person) who can monitor symptoms during the acute withdrawal period (i.e., 3–5 days) and support adherence to medications
- Any other medical or social condition that, in the treating clinician’s best judgment, would present serious risks to patient safety if alcohol withdrawal was managed on an outpatient basis

Note: Patients who do not have support from family or community or who are unstably housed due to poverty and systematic barriers should not be denied treatment. If inpatient treatment is not an option due to scarcity of beds or patient preference, patients with minimal social supports should be accommodated and treated through alternative strategies such as daily clinic visits, home visits, connection to a local pharmacist, or virtual care. If benzodiazepines are prescribed for outpatient use, consider a short-term, tapered schedule (5–7 days), daily dispensing, and blister packaging. A patient’s history of reliability and adherence to clinical recommendations should be considered as a factor in this decision.



Inpatient withdrawal management in a hospital or specialized facility should be considered for patients who do not meet the criteria specified above, who have any other contraindications to outpatient management as per the clinical judgment of the treating health care provider, or who express a preference for inpatient withdrawal management. Those who experience significant social and economic marginalization, live in poverty, or have severe comorbid conditions and acute health concerns are likely to receive safer care in an inpatient setting where they can be monitored and supported during their treatment for alcohol withdrawal. Alternatively, in communities where they are available, medically supervised outpatient withdrawal management programs (e.g., home detoxification programs involving daily visits from care team, outpatient day programs) may be considered if feasible and appropriate.

#### **4.4.i.1 Absent to Mild Withdrawal Symptoms**

Patients diagnosed with mild to moderate AUD (per DSM-5-TR criteria) may experience negligible or minor withdrawal symptoms on cessation of alcohol use. In this case, some patients may choose supportive care (e.g., supportive environment; minimal interpersonal interactions; adequate nutrition and hydration; encouragement and positive reinforcement; referrals to community resources) alone or initiation of AUD pharmacotherapy (e.g., naltrexone, acamprosate) to support long-term treatment goals (i.e., safer alcohol consumption, reduced drinking, or abstinence).

There is a lack of consensus and clear guidance regarding outpatient management of patients experiencing mild withdrawal symptoms. Practice guidelines tend to advocate provision of supportive care alone until withdrawal symptoms subside.<sup>258,302</sup> This is based on early studies that found supportive care was sufficient for approximately 75% of patients who had no comorbid complex medical conditions.<sup>303,304</sup> In view of these findings, patients with PAWSS < 4 who prefer to begin withdrawal without the use of prescription pharmacotherapies should be provided with necessary information and referrals, and monitored frequently. Over-the-counter pain relievers, anti-emetics, and anti-diarrheal medications may also be recommended for the management of mild symptoms.

#### 4.4.i.2 Mild to Moderate Withdrawal Symptoms

Studies have demonstrated that withdrawal management can be provided safely in outpatient settings to most patients with AUD.<sup>295,297,298,301</sup> Patients who are at low risk of developing severe complications of withdrawal (e.g., PAWSS < 4) and who have no other concurrent conditions or complications that would require inpatient management ([Box 7](#)) can be offered outpatient withdrawal management. Suggestions for how to provide outpatient management are listed below ([Box 8](#)).

Adequate management of withdrawal symptoms, including pharmacotherapy when appropriate, can increase the likelihood that patients will achieve their treatment goals. Thus, clinicians may also consider writing a prescription for pharmacotherapy that the patient can fill if needed, to avoid destabilizing delays in managing any significant withdrawal symptoms that emerge. Patients should be advised to contact their health care provider if this occurs. Community pharmacists can also be an important source of support and guidance for patients experiencing unexpected withdrawal symptoms. See [Pharmacotherapies for Withdrawal Management](#) for more information.

## Box 8. Providing Outpatient Withdrawal Management

### PLANNING

- Assess and identify patient's treatment goals.
- Schedule withdrawal management in consideration of available coverage and patient circumstances. Starting treatment on a weekend may minimize disruption to a patient's work. If weekend service is unavailable, schedule treatment for Monday or Tuesday to ensure access to service in the following days.
- Provide patients with a phone number or alternative contact that they can call in the event of an emergency.
- Where possible, request that a reliable person (e.g., family member, friend, caregiver, pharmacist, community support person, peer support worker) is available to provide support, help with treatment schedules, track symptoms and response to medications, and accompany or transport the patient to appointments. If not, arrange for virtual follow-up support (e.g., secure phone or video calls).
- Provide patients and family members/caregivers (with patient consent) educational resources detailing withdrawal symptoms, medications, side effects, and safety issues, as well as resources about AUD and family support.
- Provide relapse prevention support as well as overdose prevention and safety planning depending on the patient's risk factors.
- Recommend over-the-counter vitamins including thiamine and folate as a prophylactic measure before and during withdrawal. Clinicians should consult the relevant formulary to determine if coverage is available for these vitamins.
- Recommend increased fluid and electrolyte intake, restricted diet consisting of mild foods, and minimal exercise.
- Review risks and benefits of natural remedies, caffeine, or any activity that increases sweating (e.g., hot baths, showers, or saunas), with respect for and understanding of the importance of cultural healing practices for some patients (e.g., sweat lodges).
- Advise patients not to drive until their withdrawal symptoms subside.

## MONITORING

- Assess the following at each daily visit:
  - Vital signs
  - Withdrawal symptoms
  - Hydration
  - Cognition
  - Emotional status
  - General physical condition
- Assess the patient daily during the acute phase of withdrawal (i.e., 3–5 days), evaluate, and adjust the follow-up schedule thereafter as appropriate. If appropriate, consider virtual care follow-up options (i.e., phone or video calls) or connection to a local pharmacist for situations where in-person visits are not feasible.
- Provide clear instructions for circumstances that require the patient to be assessed in-person (e.g., if withdrawal symptoms worsen).
- Provide encouragement and referrals to community resources, support groups, or employee assistance programs, as appropriate.

## FOLLOW-UP

- Reassess patient's response to the treatment plan and their self-identified treatment goals regularly.
- If the patient has a goal of abstinence, monitor for return to alcohol use, and collaboratively explore and address any cause of return to alcohol use.
- If the patient has a goal of reduced alcohol consumption, continue to monitor alcohol use, offer pharmacotherapy and psychosocial interventions (see [Ongoing Care—Pharmacotherapy](#) and [Ongoing Care—Psychosocial Treatment Interventions](#)) to support self-efficacy for lower risk alcohol consumption.
- Collaboratively explore and address the cause of any alcohol use that exceeds the patient's self-identified goals.
- Consult an addiction specialist if needed, where available (see [Appendix 6: Consultation Services](#) for programs offering consultation with or referral to addiction specialists).

## 4.4.ii Inpatient Withdrawal Management

Approximately 20% of patients with AUD will require hospitalization or inpatient withdrawal management due to an increased risk of serious complications.<sup>297,298</sup> Clinicians should consult a specialist or refer patients to inpatient care if a patient is at risk of developing severe withdrawal complications. Patients located in regions that do not have dedicated inpatient withdrawal management facilities should be admitted to hospital.<sup>293,294,305</sup> For guidance on inpatient withdrawal management and managing severe alcohol withdrawal symptoms (e.g., tonic-clonic seizures, delirium tremens), see the American Society of Addiction Medicine's [Clinical Practice Guideline on Alcohol Withdrawal Management](#) and the National Institute for Health and Care Excellence's [Alcohol Use Disorders: Diagnosis and Clinical Management of Alcohol-Related Physical Complications](#).

Outpatient management of patients at high risk for severe complications is not advised.<sup>258,306</sup> If a patient has a high risk of severe withdrawal complications (e.g., PAWSS  $\geq 4$ ), but inpatient treatment is not feasible due to patient preference or lack of service availability, clinicians should arrange for community-based monitoring and support during treatment (e.g., home withdrawal programs, intensive outpatient programs, connection with a community pharmacist, involvement of family members, friends, caregivers, or community support person). Review the risks of sudden or unsupervised withdrawal from alcohol with the patient and offer to create a care plan focused on their safety that includes ensuring that they are aware of the need to seek immediate emergency assistance if any withdrawal complications are experienced. Monitor patient closely during the withdrawal period (e.g., daily phone calls, frequent clinical visits).

### 4.4.ii.1 Managed Alcohol for Inpatient Withdrawal Management

Managed alcohol programs (MAPs) are a harm reduction intervention, supported by a limited body of evidence, that aim to minimize the adverse personal and societal effects of severe AUD, particularly as experienced by individuals with chronic and severe AUD who may be experiencing homelessness or are unstably housed.<sup>307,308</sup> Managed alcohol provision typically involves dispensing individually-tailored doses of alcohol to clients at regular intervals in order to regulate alcohol intake, minimize the risk of developing severe alcohol withdrawal symptoms,

and reduce or eliminate the need for consuming non-beverage alcohol (e.g., hand sanitizer, mouthwash, rubbing alcohol, hair spray).<sup>307</sup> Some patients may express a preference for participating in a MAPS in lieu of standard withdrawal management. For more details, see [Managed Alcohol Programs](#).

#### 4.4.iii Nutritional Supplements During Withdrawal Management

Nutritional support is an important adjunct treatment during withdrawal management. Clinicians should assess patient nutrition and identify any fluid imbalances or electrolyte deficiencies. Clinical advice on how to correct any imbalances or deficiencies should be offered, including suggesting vitamin and mineral supplementations as needed. Multivitamin supplementation with thiamine (100-200mg), folic acid (1mg) and vitamin B6 (2mg) can be offered to patients with high-risk drinking levels or AUD diagnosis.<sup>309</sup> Land-based practices (e.g., water ceremony, hunting, and harvesting balanced and nourishing foods) may help support a patient's nutritional requirements and should be encouraged, if appropriate.

##### 4.4.iii.1 Thiamine

Thiamine deficiency is common in people with AUD,<sup>271</sup> resulting from inadequate dietary intake, malabsorption of thiamine, increased thiamine requirements, decreased storage capabilities, or impaired thiamine utilization.<sup>309,310</sup> Thiamine deficiency may lead to Wernicke's encephalopathy, which progresses to a permanent disorder, Korsakoff's syndrome, if untreated.<sup>309</sup> Prophylactic oral thiamine 100-200mg should be given to patients in outpatient settings who are malnourished/at risk of malnourishment, have decompensated liver disease, or are in acute withdrawal; or before and during a planned medically-assisted withdrawal.<sup>311</sup> Offer 200–300mg of parenteral thiamine (intravenously or intramuscularly) to patients with suspected Wernicke's encephalopathy; offer prophylactic parenteral thiamine to patients who present to emergency department or are admitted to hospital and have malnourishment/risk of malnourishment or decompensated liver disease.<sup>311</sup> Parenteral thiamine should be given for a minimum of 5 days unless Wernicke's encephalopathy is excluded, followed by oral thiamine.<sup>311</sup>

#### 4.4.iii.2 Folic acid

Low levels of folic acid concentrations are commonly reported in people with AUD.<sup>309</sup> Low dietary intake of folic acid can cause severe megaloblastic anemia within 5 weeks in people with AUD, with folic acid stores beginning to deplete within days of last intake.<sup>271</sup> Severe anemia is associated with weakness, vertigo, tinnitus, fatigue, drowsiness, and irritability; heart failure and shock may also occur.<sup>309</sup>

#### 4.4.iii.3 Vitamin B6

Vitamin B6 deficiency occurs frequently in people with AUD, which can contribute to behavioural changes, neurological disorders, peripheral neuropathy, and dermatological disorders.<sup>309</sup> Vitamin B6 can be consumed as part of a daily multivitamin; large doses (200mg) of vitamin B6 should be avoided due to the risk of ataxia.<sup>309</sup>

## 4.5 Pharmacotherapies for Withdrawal Management

### In this section:

- Benzodiazepines
- Carbamazepine
- Gabapentin
- Valproic acid
- Clonidine

This section reviews the evidence on the efficacy and safety of the following medications commonly used to manage alcohol withdrawal symptoms: benzodiazepines, anticonvulsants, and clonidine. Refer to [Table 14](#) for a summary comparison of withdrawal management pharmacotherapies. Other medications with insufficient evidence for withdrawal management (e.g., baclofen<sup>312,313</sup>) were not included.

### 4.5.i Benzodiazepines

Benzodiazepine medications are the most widely-used pharmacotherapy in the treatment of alcohol withdrawal,<sup>265,290,297,314-318</sup> with strong evidence from multiple systematic reviews demonstrating their superior efficacy in the prevention of delirium tremens and seizures compared to placebo and alternative therapies including anticonvulsants and antipsychotics.<sup>319-321</sup> The studies included in this summary contain a mix of inpatient and outpatient settings.

To date, no systematic review has conclusively established that any one class of benzodiazepine is superior to another for alcohol withdrawal management, although a 2010 Cochrane review and meta-analysis (N = 64, n = 4,309) reported that chlordiazepoxide may be marginally more effective than other benzodiazepines in reducing seizures, while diazepam performed better than other benzodiazepines in reducing delirium tremens, though neither comparison reached significance. Benzodiazepines (i.e., diazepam, chlordiazepoxide, lorazepam) performed similarly in

terms of reducing symptom severity, as measured by the CIWA-Ar.<sup>321</sup> A 2021 meta-analysis (N = 9, n = 423) that examined the effectiveness of diazepam compared to non-benzodiazepine treatments (i.e., carbamazepine, clomethiazole, oxcarbazepine,  $\gamma$ -hydroxybutyric acid) found no significant difference

**Long-acting benzodiazepines (e.g., chlordiazepoxide, diazepam) are preferred for the general adult population. Shorter-acting benzodiazepines (e.g., lorazepam or oxazepam) are preferred for older adults and patients with cirrhosis or severe liver dysfunction.**

in decreases in CIWA-Ar scores between treatment groups.<sup>282</sup> Therefore, other factors such as provider experience, duration of action (i.e., short- versus long-acting), dosing schedule, patient's health history (e.g., history of hepatic dysfunction), drug coverage and availability, and potential for non-medical use may guide medication selection. For example, lorazepam or oxazepam are the preferred benzodiazepine for the treatment of alcohol withdrawal in older adults and in patients with cirrhosis or severe liver dysfunction, while long-acting benzodiazepines (e.g., chlordiazepoxide, diazepam) may be preferred in other populations.<sup>273</sup> While all benzodiazepines are metabolized by the liver, lorazepam and oxazepam have no active metabolites, an intermediate half-life, and are less prone to accumulation compared to long-acting benzodiazepines. As older adult patients and patients with cirrhosis or severe liver dysfunction experience a decrease in medication clearance and an increase in accumulated metabolites, long-acting benzodiazepines may result in oversedation<sup>273</sup> and should be avoided.

There is growing evidence to support the use of symptom-triggered benzodiazepine dosing instead of a fixed-dose benzodiazepine schedule for the treatment of alcohol withdrawal. A 2019 meta-analysis (N = 6 RCTs, n = 664) found that the symptom-triggered benzodiazepine approach lowered the total dosage and treatment duration time compared to fixed-dose benzodiazepine



treatment; however, the majority of included RCTs enrolled low-risk participants who did not develop withdrawal symptoms and, as a result, did not receive benzodiazepines in the symptom-triggered study arm.<sup>322</sup> A subsequent 2020 RCT (N = 96) demonstrated similar results, finding individuals prescribed symptom-triggered benzodiazepines had a significantly lower total benzodiazepine (i.e., chlordiazepoxide) dose during 1 week of alcohol withdrawal (170.5mg vs. 286.5mg;  $p < .001$ ) and a shorter duration of alcohol withdrawal (3.9 days vs. 6.4 days;  $p < .001$ ) compared to those prescribed a fixed-dose benzodiazepine regimen.<sup>323</sup> Median CIWA-Ar scores were comparable between groups, suggesting withdrawal symptoms were effectively managed with both symptom-triggered and fixed-dose benzodiazepines. Individuals with delirium tremens in the symptom-triggered group received similar doses of chlordiazepoxide to the fixed schedule group (635mg vs. 500mg;  $p = .583$ ), while individuals without delirium tremens in the symptom-triggered group required a significantly lower total chlordiazepoxide dose compared to the fixed schedule group (88.5mg vs. 255.7mg;  $p < .0001$ ). The results from this study support the use of symptom-triggered benzodiazepine treatment for alcohol withdrawal, as it reduces unnecessary benzodiazepine use while avoiding withdrawal-related complications.<sup>323,324</sup>

A 2020 prospective cohort study (n = 22,899 hospitalizations), which assessed changes in medication use and service outcomes for patients hospitalized with alcohol withdrawal syndrome following the implementation of a benzodiazepine-sparing order set found favourable outcomes.<sup>324</sup> The printed order set included treatment pathways based on PAWSS or CIWA-Ar scores, reduced benzodiazepine dosing scales, and non-benzodiazepine medications (e.g., gabapentin, valproic acid, clonidine, dexmedetomidine). Following implementation of the new printed order, there was a significant decrease in prescriptions for benzodiazepines among patients hospitalized for alcohol withdrawal (78.1% of patients before vs. 60.7% of patients after;  $p < .001$ ) and in the mean total benzodiazepine (i.e., lorazepam) dosage (19.7mg before vs. 6.0mg after;  $p < .001$ ). The use of the benzodiazepine-sparing printed order set was associated with reduced intensive care unit use (adjusted rate ratio [ARR]: 0.71; 95%CI: 0.56 to 0.89;  $p = .003$ ) and hospital length of stay (ARR: 0.71; 95%CI: 0.58 to 0.86;  $p < .001$ ) when compared to hospitalizations that did not use the benzodiazepine-sparing printed order. This study suggests that initiatives to decrease benzodiazepine use among patients with alcohol withdrawal syndrome is effective for managing withdrawal while potentially improving patient safety and reducing service utilization.

**Benzodiazepine treatment should be short-term and limited to the acute withdrawal phase. Long-term use is not recommended.**

Regardless of benzodiazepine type, the duration of treatment should be short-term and limited to the acute phase of alcohol withdrawal, with a taper schedule determined by the individual's response to treatment

(typically 5–7 days). Long-term benzodiazepine use is not recommended. The risks and side effects of benzodiazepines increase with duration of use and escalating doses.<sup>325</sup> Benzodiazepines have a high potential for non-medical use and dependence; physiological dependence can develop quickly.<sup>326</sup> Short and long-term benzodiazepine use is positively associated with harms such as persistent memory or other neurocognitive deficits,<sup>327-329</sup> motor vehicle collisions,<sup>330,331</sup> increase in severity of anxiety and PTSD,<sup>332</sup> and suicidal thoughts and behaviours.<sup>333</sup> Older adults, frail patients, and those with hepatic dysfunction may be at particular risk of developing side effects from benzodiazepines.<sup>289,290</sup> As the combined use of benzodiazepines and alcohol, opioids, or other CNS depressants can cause respiratory depression and death, the importance of abstaining from alcohol, opioids, or other CNS depressants as well as taking the medication as directed must be emphasized to patients and families or caregivers. To prevent overdose or non-medical use, discuss a safety plan with the patient exploring methods that can mitigate their triggers and risk for relapse and who they can draw on for support when having substance use cravings. If benzodiazepines are prescribed for outpatient care, daily or frequent dispensing schedules and blister packaging can be considered to mitigate risks if appropriate. Potential risks associated with non-medical use and diversion of benzodiazepines should also be considered. Medication administration support can be provided from a pharmacy during outpatient care if available.

#### 4.5.ii Anticonvulsants

In view of the side effects and risks related to benzodiazepines, there is growing interest in non-benzodiazepine treatments for alcohol withdrawal.<sup>334</sup> Anticonvulsants, also known as antiseizure or antiepileptic medications, are one alternative to benzodiazepines and are used to alleviate alcohol withdrawal symptoms. Despite their widespread use, there is limited data on the safety and efficacy of anticonvulsants for alcohol withdrawal.<sup>335</sup>

A 2021 meta-analysis (N = 24, n = 2,223) of RCTs conducted in inpatient, outpatient, and emergency department settings found anticonvulsant medications<sup>z</sup> were not superior compared to placebo or benzodiazepines for alcohol withdrawal.<sup>336</sup> In terms of effectiveness, there were no significant differences between anti-convulsant medications for seizures, delirium tremens, or CIWA-Ar scores after 4 days compared to placebo or benzodiazepines. When anticonvulsant monotherapy was compared to combined anticonvulsant and benzodiazepine treatment, there was a similar frequency of delirium tremens between treatments. Anticonvulsants increased the odds (OR: 3.50, 95% CI: 1.32 to 9.28;  $p = .012$ ) of requiring rescue medication compared to benzodiazepines but had reduced odds (OR: 0.49, 95% CI: 0.29 to 0.83) compared to a placebo. Dropout was significantly increased for anticonvulsants compared to placebo (OR: 1.86, 95% CI: 1.05 to 3.28;  $p = .034$ ) but there was no difference in dropout compared to benzodiazepines. Adverse events were similar between anticonvulsants versus placebo and between combined anticonvulsants and benzodiazepines versus benzodiazepines alone. All findings in this meta-analysis were rated as low or very low quality, due to the risk of bias (e.g., poor methodological reporting, high dropout rates) in the included studies and the lack of studies published since 2015. Moreover, most RCTs included participants with only mild alcohol withdrawal; thus, few participants required pharmacological treatment for alcohol withdrawal. Consequently, findings may not be applicable for those with moderate to severe alcohol withdrawal symptoms.<sup>336</sup>

#### 4.5.ii.1 Carbamazepine

Carbamazepine has been used in Europe for over 35 years to manage symptoms of alcohol withdrawal,<sup>337</sup> and has been found relatively safe and effective for the management of alcohol withdrawal in a number of RCTs.<sup>335,338-342</sup> Some advantages of carbamazepine are that it is non-sedating, does not interact with alcohol, and has no reported potential for non-medical use or diversion.

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- z The following anti-seizure medications were included in this meta-analysis: brivaracetam, cannabidiol, carbamazepine, eslicarbazepine acetate, ethosuximide, fosphenytoin sodium, gabapentin, lacosamide, lamotrigine, levetiracetam, oxcarbazepine, paraldehyde, perampanel, phenytoin, pregabalin, rufinamide, sodium valproate, stiripentol, tiagabine, topiramate, valproic acid, vigabatrin, and zonisamide.

To date, 5 randomized trials conducted in inpatient settings (n = 422) have demonstrated that carbamazepine is equivalent<sup>338-341</sup> or superior<sup>342</sup> to benzodiazepines for the reduction of withdrawal symptom severity. Similar results were demonstrated in a 2002 RCT conducted in an outpatient setting, where 136 participants were randomized to receive a fixed-dose taper over 5 days of either carbamazepine (800mg on day 1 tapering to 200mg by day 5) or lorazepam (6–8mg on day 1 tapering to 2mg by day 5).<sup>343</sup> The authors reported a significant difference in physician-assessed withdrawal severity over time ( $p = .007$ ) and at day 7 post-treatment ( $p = .01$ ) favouring carbamazepine.<sup>343</sup> Furthermore, evaluation of post-treatment drinking behaviour found that participants who received lorazepam were three times more likely to return to drinking immediately following treatment than those who received carbamazepine ( $p = .044$ ). In all trials conducted to date, there were no reports of safety issues, and carbamazepine was well tolerated with no difference between treatment arms in dropout rates due to side effects.<sup>337</sup> A 2010 Cochrane review and meta-analysis (N = 46, n = 4,076) concluded that, of all non-benzodiazepine anticonvulsants studied to date, carbamazepine is the only medication that may be more effective than benzodiazepines in reducing the severity of alcohol withdrawal symptoms.<sup>335</sup>

Side effects of carbamazepine are generally mild and temporary. The aforementioned 2010 meta-analysis reported that carbamazepine can have side effects in up to 18% of patients; however, the authors also noted that the treatment was generally well-tolerated, with fewer than 2% of trial drop-outs due to intolerable side effects.<sup>335</sup> The most commonly reported side effects in carbamazepine RCTs were pruritus (6.9–18%), dizziness (11.5%), and nausea and vomiting (3.8–10.3%), while fewer than 3% of participants experienced mental confusion, drowsiness, and rash.<sup>335</sup> As some of these side effects can mimic or mask symptoms of alcohol withdrawal, caution should be exercised in distinguishing between withdrawal symptoms and medication side effects prior to dose adjustment. At higher doses (> 1200mg/day) and with longer treatment duration (e.g., for seizure disorders), carbamazepine has been associated with rare blood dyscrasias and Stevens Johnson Syndrome<sup>344</sup>; however, these adverse events have not been reported in any RCTs of carbamazepine for alcohol withdrawal.<sup>337</sup> Importantly, pharmacogenetic studies have shown that some individuals of Asian

ethnicity<sup>aa</sup> are at increased risk of severe adverse events due to a higher prevalence of a genetic variant for carbamazepine toxicity (HLA-B\*15:02).<sup>345</sup> Prescribing carbamazepine should be avoided in patients of Asian ethnicity unless genetic testing indicates this allelic variant is not present. This allele is common globally<sup>ab</sup> and has been found in Europeans, Chinese, Japanese, North Americans of mixed ancestries, and South Americans.<sup>347</sup> Clinicians should consider monitoring patients for adverse reactions to carbamazepine if there is an elevated risk of carrying the HLA-B\*15:02 or HLA-A\*31:01 allele. Carbamazepine has known drug–drug interactions with many other medications, which should be carefully reviewed and considered before prescribing. For more information, see the [Lexicomp Drug Interactions](#) online tool from UpToDate.

#### 4.5.ii.2 Gabapentin

Gabapentin has a growing evidence base supporting its efficacy and safety for outpatient management of alcohol withdrawal in patients at low risk of complications.<sup>348,349</sup> Results from two 2020 systematic reviews indicate that gabapentin is effective in reducing the severity of alcohol withdrawal symptoms. The first systematic review, which included a meta-analysis (N = 16, 7 RCTs focused on alcohol withdrawal, n = 318), showed that gabapentin is effective in reducing the severity of alcohol withdrawal symptoms compared to treatment as usual (i.e., benzodiazepines, phenobarbital) and placebo (Hedges'  $g^{ac}$  = 0.29, 95% CI: 0.03 to 0.55;  $p$  = .0296).<sup>348</sup> A second 2020 systematic review (N = 34, n = 2,338)

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- aa The association between the HLA-B\*15:02 allele and carbamazepine-induced Stevens-Johnson syndrome and toxic epidermal necrolysis has been mostly found in Han Chinese populations<sup>345</sup>; however, the FDA recommends genetic testing for all individuals of Asian background due to the relatively high incidence of the HLA-B\*1502 allele in these populations.<sup>346</sup> The prevalence of the HLA-B\*15:02 allele ranges from 15% in Hong Kong, Thailand, Malaysia, Vietnam, and parts of the Philippines, 10–13% in Taiwan and Singapore, 4% in North China, 2–4% in South Asia, to less than 1% in Japan and Korea and in individuals who are not of Asian ethnicity.<sup>347</sup>
- ab The prevalence of the HLA-A\*31:01 allele ranges from 15% in Japanese, Indigenous peoples of North America, South Indian, and some Arabic individuals, up to 10% in Han Chinese, Korean, European, Latin American, and other Indian individuals, to  $\leq$  5% in African-Americans, Thai, Taiwanese, and Chinese (Hong Kong) individuals.<sup>347</sup>
- ac Hedges'  $g$  is a measure of effect size. A result of  $< 0.20$  is a small effect size, between 0.20 and 0.50 is a medium effect size, and  $> .50$  is a large effect size.

examining non-benzodiazepine medications for alcohol withdrawal concluded that there was moderate-quality evidence to support the use of gabapentin compared to benzodiazepines to produce a similar or better reduction in the severity of withdrawal symptoms, with a higher dose (i.e., 1200mg/day for the first days) potentially more effective than a lower dose (i.e., 600mg/day). The authors suggest that gabapentin should be the first alternative treatment for patients with moderate to severe alcohol withdrawal where there are concerns for prescribing benzodiazepines (e.g., risk of concurrent use of CNS depressants, diversion). This may be particularly relevant in the context of virtual health, where patients cannot be closely monitored during alcohol withdrawal treatment.

Results from 2009<sup>78</sup> (n = 100) and 2013<sup>79</sup> (n = 26) RCTs indicate that gabapentin (1200mg per day) is as effective as benzodiazepines for the outpatient management of mild alcohol withdrawal symptoms and may confer additional benefits in terms of greater daytime alertness and sleep quality, and less anxiety and mood disturbances.<sup>350,351</sup> Additional support for gabapentin's efficacy is provided from an open-label trial among 27 inpatients experiencing mild to moderate withdrawal symptoms, which showed that a higher dosage of gabapentin (1200mg BID, tapered by 600mg daily) had effects comparable to those of phenobarbital, with similar outcome scores between the two treatments.<sup>352</sup> In addition, a 2010 observational study of 37 inpatients experiencing acute withdrawal showed that two hours after the administration of 800mg of gabapentin, 73% (27) patients showed a significant reduction in symptom severity as measured by CIWA-Ar scores (17.3 to 8.0;  $p < .001$ ).<sup>353</sup>

In addition to being a treatment option for withdrawal management, gabapentin is recommended as a second-line pharmacotherapy for ongoing care AUD treatment. A more comprehensive review of safety considerations for gabapentin, including non-medical use, diversion, physiological dependence, and overdose risk can be found in the [Ongoing Care—Pharmacotherapy](#) section.

#### **4.5.ii.3 Valproic acid**

There is limited evidence to support the efficacy of valproic acid for treating alcohol withdrawal. A 2020 systematic review (N = 34, n = 2,338) examining non-benzodiazepine medications for alcohol withdrawal concluded that there

was low quality evidence to support the use of valproic acid for the treatment of alcohol withdrawal compared to benzodiazepines.<sup>354</sup> Most RCTs conducted to date have been small and underpowered.<sup>355</sup> Only 2 of 6 published trials reported a statistically significant difference in favor of valproic acid for the treatment of alcohol withdrawal, and these differences were of marginal clinical significance.<sup>355</sup> Both trials found that valproic acid results in a more rapid and consistent decline in the severity of withdrawal symptoms compared to a benzodiazepine (lorazepam and chlordiazepoxide)<sup>356,357</sup>; however, due to small sample sizes, an adequate evaluation of safety (e.g., prevention of severe symptoms, seizures, or delirium tremens) and adverse events could not be performed.<sup>355</sup> The most commonly reported side effect in clinical trials was gastrointestinal upset.<sup>355</sup> In terms of safety, valproic acid does not have potential for non-medical use or diversion, nor does it potentiate the effects of alcohol or other CNS depressants (e.g., opioids, benzodiazepines) when taken together.<sup>358</sup>

#### 4.5.iii Clonidine

Clonidine is a centrally acting  $\alpha$ -adrenergic agonist that can suppress persistent noradrenergic symptoms (e.g., hypertension, tachycardia) associated with mild alcohol withdrawal that may be prescribed as a standalone or adjunct pharmacotherapy. When prescribed as a standalone treatment, clonidine should only be used for treating mild withdrawal symptoms in patients who are at low risk of developing severe complications of withdrawal (e.g., PAWSS < 4).<sup>359</sup> Two RCTs have reported that clonidine (at doses of 0.2–0.6mg per day) is as effective as the benzodiazepine chlordiazepoxide in the management of mild to moderate withdrawal symptoms, with advantages in control of sympathetic symptoms and reductions in patient anxiety.<sup>360,361</sup> Both trials excluded patients with a history of withdrawal-related seizures.<sup>360,361</sup> There have been no reports of safety issues with concomitant administration of clonidine with other medications. Therefore, clonidine can also be considered as an adjunct medication for patients who are prescribed benzodiazepines, carbamazepine, gabapentin, or other anticonvulsants, as it may provide additional benefits in managing withdrawal symptoms via a different mechanism of action than these drugs.<sup>362</sup>

## 4.5.iv Section Summary and Recommendations

### 4.5.iv.1 Withdrawal Management for Patients at Low Risk of Severe Complications

Based on available evidence, the guideline committee recommends non-benzodiazepine medications as the preferred approach for the outpatient management of mild to moderate withdrawal symptoms in patients at low risk of severe complications. Carbamazepine<sup>335,338-341</sup> and gabapentin<sup>335,350,351</sup> have been shown to be safe and effective for the management of mild to moderate withdrawal symptoms in comparison to placebo. The use of clonidine as an adjunctive option for mild to moderate withdrawal symptoms is also supported by moderate quality evidence<sup>360,361</sup>; however, clonidine should only be prescribed as a standalone pharmacotherapy for patients with mild withdrawal symptoms.

There is insufficient evidence showing that gabapentin, carbamazepine, and clonidine are effective for preventing seizures or delirium tremens; however, these medications are safe and effective for treating mild to moderate withdrawal symptoms.

There is limited evidence to support the efficacy of valproic acid for the treatment of alcohol withdrawal.<sup>355</sup> Thus, while this medication may still be commonly used for alcohol withdrawal management in some care settings, the committee recommends that it should only be considered when all other pharmacotherapy options are contraindicated.

An established body of evidence supports the safety and effectiveness of outpatient withdrawal management for the majority of patients (80%) with AUD.<sup>297,298,363</sup> Outpatient management is generally safe, effective, and more cost-effective than inpatient treatment,<sup>298,299</sup> and may be less disruptive to patients' work and family life.<sup>300</sup> Reviews from the 1990s report that more than 70% of patients enrolled in outpatient withdrawal management complete treatment and 50% of these patients remain engaged in ongoing addiction care.<sup>295,301</sup>



## Recommendation 6

For patients at low risk of severe complications of alcohol withdrawal (e.g., PAWSS < 4), clinicians should consider offering non-benzodiazepine medications such as gabapentin, carbamazepine, or clonidine for withdrawal management in an outpatient setting (e.g., primary care, virtual).

**MODERATE** Quality of Evidence (gabapentin)  
**LOW** Quality of Evidence (carbamazepine, clonidine)

**STRONG** Recommendation

### Remarks

- Selection of an appropriate medication should be made through shared decision-making by patient and provider in consideration of a patient's goals, needs, and preferences.
- Contraindications, side effects, feasibility (dosing schedules, out-of-pocket costs), and patient history should also be considered when selecting a medication.
- Gabapentin is contraindicated in patients with hypersensitivity to this medication. Caution is advised for patients with renal impairment. Gabapentin should not be combined with opioids.
- Carbamazepine is contraindicated in patients with hepatic disease, bone marrow depression, serious blood disorder, and atrioventricular heart block.
- Monitor patients for adverse reactions to carbamazepine if there is an elevated risk of carrying the HLA-B\*15:02 or HLA-A\*31:01 allele.<sup>345,347</sup>
- Clonidine is contraindicated in patients with sinus node function impairment, severe bradyarrhythmia, and galactose intolerance. Caution is advised for patients with a history of hypotension.
- Clonidine may be prescribed as a standalone (mild symptoms only) or adjunct pharmacotherapy.
- In addition to a PAWSS score < 4, candidates for outpatient withdrawal management should meet the following criteria:
  - No contraindications such as severe or uncontrolled comorbid medical conditions, serious psychiatric conditions, co-occurring severe substance use disorders other than tobacco use, or pregnancy.
  - Ability to follow-up for first 3–5 days in-person or through virtual care.
  - Ability to take oral medications.
  - Stable accommodation and reliable support person (e.g., family member, friend, caregiver, pharmacist, community support person) for providing support and monitoring symptoms during acute withdrawal period (i.e., 3–5 days).
- For patients who do not meet these criteria, support and guidance from an addiction specialist or team may be required, and inpatient management can be considered. Patients with a PAWSS score < 4 who prefer inpatient treatment should be offered a referral if inpatient treatment is available.
- Assess patient's treatment goals and social determinants of health and offer patients a referral to psychosocial and community resources informed by their goals (see [Ongoing Care](#)—Psychosocial Treatment Interventions and [Community-Based Supports and Programs](#)).

## Remarks *Continued...*

- Offer oral thiamine (100-200mg) to patients with high-risk drinking levels or AUD. Encourage vitamin supplementation for folic acid (1mg) and vitamin B6 (2mg).
- The quality of evidence for this recommendation was rated as moderate because multiple meta-analyses and RCTs have demonstrated the safety and effectiveness of carbamazepine and gabapentin for managing withdrawal in patients at low risk of developing severe complications from alcohol, while limited evidence supports the use of valproic acid to treat withdrawal. Clonidine may be safe and effective as a standalone treatment for mild withdrawal symptoms and as an adjunct pharmacotherapy to benzodiazepines, carbamazepine, gabapentin, or other anticonvulsants. The use of these non-benzodiazepine medications reduces the risks and side effects associated with benzodiazepine use. Additionally, evidence indicates that outpatient withdrawal management is safe and effective for up to 80% of patients with AUD, with 70% of patients enrolled completing treatment and 50% of those patients remaining engaged in ongoing AUD care.
- The strength of this recommendation was rated as strong based on the quality of the evidence, working group consensus, feasibility, cost-effectiveness of outpatient treatment, and the benefits of reducing the risks associated with benzodiazepine use in outpatient settings.

### 4.5.iv.2 Withdrawal Management for Patients at High Risk of Severe Complications

This guideline recommends using a benzodiazepine regimen for patients at high risk of developing severe complications of withdrawal, ideally prescribed in an inpatient setting where patients can receive treatment under close observation. Multiple systematic reviews have reported high quality evidence that benzodiazepines are more effective than placebo and other active treatments for the suppression of severe withdrawal symptoms and prevention of delirium tremens and seizures.<sup>319-321</sup>

Benzodiazepines are generally not a preferred option for outpatient withdrawal management due to their well-documented side effects, tendency to potentiate the effects of alcohol if used concurrently, and potential for non-medical use, diversion, and dependence.<sup>258</sup>

**Although not preferred, if benzodiazepines are prescribed for outpatient withdrawal management, the following measures should be considered: prescribing a short course prescription (5–7 days) with a tapered schedule, daily dispensing from a pharmacy, and frequent in-person or virtual clinical assessments to closely monitor side effects, symptoms, and alcohol use/other substance use, and to make dose adjustments as needed.**

## Recommendation 7

**For patients at high risk of severe complications of withdrawal (e.g., PAWSS  $\geq$  4), clinicians should offer a short-term benzodiazepine prescription ideally in an inpatient setting (i.e., withdrawal management facility or hospital). However, where barriers to inpatient admission exist, benzodiazepine medications can be offered in outpatient settings if patients can be closely monitored.**

HIGH Quality of Evidence

STRONG Recommendation

### Remarks

- Selection of an appropriate benzodiazepine should be made through shared decision-making by patient and provider in consideration of a patient's goals, needs, and preferences.
- Contraindications, side effects, feasibility (dosing schedules, out-of-pocket costs), and patient history should also be considered when selecting a benzodiazepine.
- Benzodiazepines may be contraindicated in some patients with severe respiratory insufficiency, abnormal liver function, sleep apnea, myasthenia gravis, and narrow angle glaucoma.
- There is potential for benzodiazepines to have drug–drug interactions with CNS depressants (e.g., alcohol, opioids) and gabapentin, leading to excess sedation, impaired psychomotor and cognitive functioning.
- If a patient has a PAWSS  $\geq$  4 but inpatient treatment is not feasible due to patient preference or scarcity of beds, clinicians should arrange for community-based monitoring and support during treatment (e.g., home withdrawal programs, intensive outpatient programs, connection with a community pharmacist, involvement of family members, friends, caregivers, or community support person) and monitor the patient closely (daily phone calls, frequent clinical visits).
- If benzodiazepines are prescribed for outpatient withdrawal management, clinicians should consider: prescribing a short course, tapered prescription (5–7 days), daily dispensing from a pharmacy, and frequent clinical visits to closely monitor side effects, symptoms, and alcohol use, and to make dose adjustments as needed.
- Assess patient's treatment goals and social determinants of health and offer patients a referral to psychosocial and community resources informed by their goals (see [Ongoing Care—Psychosocial Treatment Interventions](#) and [Community-Based Supports and Programs](#)).
- Offer oral thiamine (100-200mg) to patients with high-risk drinking levels or AUD. Thiamine should be offered intravenously or intramuscularly (200-300mg) in cases of suspected severe thiamine deficiency or Wernicke's encephalopathy. Encourage vitamin supplementation for folic acid (1mg) and vitamin B6 (2mg).
- The quality of evidence for this recommendation was rated high based on multiple systematic reviews supporting the use of benzodiazepines to manage severe withdrawal symptoms and prevent seizures and delirium tremens.<sup>319-321</sup>
- The strength of this recommendation was rated strong based on the quality of evidence, working group consensus, and benefits of reducing the risks associated with benzodiazepines.

## 4.6 Withdrawal Management in Youth Patients

Withdrawal symptoms on cessation or significant reduction of alcohol use are relatively rare among youth patients (aged 12–19 years) with AUD.<sup>364</sup> It is estimated that 5 to 10% of youth with an AUD will experience withdrawal symptoms of any severity,<sup>364</sup> and only a subset of these individuals will require pharmacological management.<sup>365</sup> Due to the relative rarity of this condition, no empirical data are available to make evidence-based recommendations for pharmacological management of alcohol withdrawal in adolescents. Practice guidelines recommend that, in rare cases where pharmacological management is necessary, approaches are generally the same for youth as for adult patients.<sup>365</sup> In cases involving youth, a consultation with an addiction medicine specialist is strongly recommended prior to initiating monitored withdrawal in an outpatient setting, even if the PAWSS < 4, as this instrument has not been validated for use in youth.

## 4.7 Withdrawal Management in Pregnant Patients

There are unique considerations for withdrawal management in pregnant individuals. The potential maternal/parental and fetal risks and benefits of pharmacotherapy must be weighed against the known risks of untreated withdrawal or continued alcohol consumption. Adding to this, very few medications have been studied in pregnant individuals, and several options that have been proven safe and effective in non-pregnant adult patients are contraindicated in pregnancy due to the risk of fetal malformations (e.g., carbamazepine).

The limited research on withdrawal management during pregnancy has been focused almost exclusively on benzodiazepine-based pharmacotherapy and has yielded conflicting results. Early case-control studies suggested that benzodiazepines were associated with increased risk of fetal malformations<sup>366</sup>; however, a 2011 meta-analysis (N = 9, n = 1,051,376) including case-control and cohort studies concluded that, overall, the available evidence did not support benzodiazepine teratogenicity.<sup>367-369</sup> These results should be considered with caution, as very few studies have been published on the topic, and there have been no randomized or quasi-randomized trials of pharmacological withdrawal management in pregnant individuals with AUD. More research is needed to accurately assess the safety and efficacy of available treatments in this population.<sup>370</sup>

Few clinical practice guidelines have made explicit recommendations for withdrawal management in pregnant individuals. The World Health Organization's 2014 [Guidelines for Identification and Management of Substance Use and Substance Use Disorders in Pregnancy](#) and the BC Centre on Substance Use, the BC Ministry of Health, and the BC Ministry of Mental Health and Addictions' 2020 [Pregnancy Supplement—Provincial Guideline for the Clinical Management of High-Risk Drinking and Alcohol Use Disorder](#) recommend that pregnant individuals with AUD should be admitted to inpatient withdrawal management facilities or hospital settings that are appropriately equipped to monitor fetal movement, fetal heart rate, and vital signs during treatment.<sup>371</sup> Pharmacotherapy with benzodiazepines, preferably a shorter-acting benzodiazepine (e.g., lorazepam, oxazepam), is recommended where indicated and appropriate, to be delivered under close observation so that dose can be titrated to severity of withdrawal symptoms (i.e., symptom-triggered protocol).<sup>258,371</sup> Gabapentin can be considered in the treatment of mild alcohol withdrawal during pregnancy, though the limited information regarding the safety of gabapentin use during pregnancy comes from its use for other indications (e.g., pain, epilepsy, mood disorders).<sup>372</sup> In the absence of clear evidence, the risks of untreated maternal/parental alcohol withdrawal symptoms, which include fetal distress, spontaneous abortion, preterm birth, and fetal demise,<sup>369</sup> must be weighed against the risks of pharmacological treatment. If pharmacological treatment is needed close to birth or for prolonged periods, referral or consult with pediatrics is advised. Medications such as benzodiazepines can complicate neonatal abstinence syndrome and be excreted in breastmilk in varying amounts depending on drug, dose, and duration. If medications are used during breastfeeding, clinicians are advised to monitor the infants for drowsiness.

## 4.8 Withdrawal Management in Older Adults

Older adults (generally, individuals 65 years of age and older<sup>ad</sup>) have an increased risk of developing complications from alcohol withdrawal due to the higher prevalence of comorbidities, generally longer drinking histories, and greater sensitivity to treatments for alcohol withdrawal. Older adults may experience alcohol withdrawal symptoms earlier than younger adults following cessation/reduction of drinking. Additionally, withdrawal symptoms often increase in severity and duration with increased age.<sup>373</sup> Those who have insufficient nutrition or some chronic illnesses (e.g., cancer) are at a higher risk of developing Wernicke's encephalopathy.<sup>374</sup> Data from the US suggest that hospitalizations for alcohol withdrawal among older adults significantly increased between 2005 and 2014, particularly among those aged 65 to 74.<sup>375</sup> Similar data was not found for Canada.

In 2019, the Canadian Coalition for Seniors' Mental Health published [Canadian Guidelines on Alcohol Use Disorder Among Older Adults](#). Their recommendations include administering PAWSS to help determine withdrawal management care pathways, using a symptom-triggered protocol based on CIWA-Ar scores when prescribing a shorter-acting benzodiazepine (e.g., lorazepam), offering a managed alcohol taper in circumstances where medical withdrawal management is not available or appropriate, and administering 200mg of parenteral thiamine intramuscularly or intravenously daily for 3–5 days.

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ad Aging has many dimensions, encompassing biological, psychological, social, and cognitive risk factors. Throughout this guideline, "older adult" refers to those 65 years of age and older. However, the guidance may be relevant for some individuals under 65 years of age, due to medical, psychological, and social contexts. Conversely, some individuals 65 years of age and older may be better suited to approaches used for adults younger than 65 years of age.

## 4.9 Withdrawal Management with Comorbid Medical Conditions

Before initiating withdrawal management, clinicians should assess patients for comorbid medical conditions that may affect alcohol withdrawal or require their own treatment. If possible, laboratory tests (e.g., comprehensive or basic metabolic profile, a hepatic panel,<sup>ae</sup> and a complete blood count) should be conducted to help guide treatment decisions. If indicated, and with a view toward public health, clinicians should consider screening for infectious diseases such as sexually transmitted infections, hepatitis, HIV, and tuberculosis (skin test). Barriers to laboratory tests or pending results (e.g., virtual care, lack of access to a local laboratory) should not prevent clinicians from initiating treatment for alcohol withdrawal.<sup>376</sup>

Common medical conditions associated with AUD include hypertension, heart diseases, hepatic diseases, and digestive problems. Increased autonomic hyperactivity caused by alcohol withdrawal can exacerbate concurrent medical conditions, particularly cardiovascular diseases. Patients with these conditions may require early aggressive autonomic symptom prevention. Clinicians should identify if patients with comorbid medical conditions take any medications that suppress autonomic symptoms (e.g., beta-adrenergic antagonists), as these medications may mask withdrawal symptom severity. The presence of comorbid medical conditions may require withdrawal management pharmacotherapies to be modified.<sup>376</sup> For example, lorazepam or oxazepam are the preferred benzodiazepine for the treatment of alcohol withdrawal for patients with cirrhosis or severe liver dysfunction because these benzodiazepines have no active metabolites, an intermediate half-life, and are less prone to accumulation compared to long-acting benzodiazepines.<sup>273,376</sup> As patients with cirrhosis or severe liver dysfunction experience a decrease in medication clearance and an increase in accumulated metabolites, long-acting benzodiazepines may result in oversedation<sup>273</sup> and should be avoided.

When treating patients with comorbid medical conditions, clinicians should consult with an appropriate specialist (e.g., cardiology, hematology, infectious diseases).<sup>376</sup> Patients with stable, controlled, comorbid medical conditions may be

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ae Clinicians should further investigate results that indicate abnormal liver function. Acute hepatitis and liver failure or decompensated cirrhosis are of particular interest in the context of AUD.

able to undergo outpatient withdrawal management as indicated by their PAWSS score, while patients with uncontrolled comorbid medical conditions should be referred to inpatient facilities, regardless of PAWSS score. See [Co-occurring Substance Use Disorders](#) for guidance on withdrawal management and AUD care in the context of co-occurring substance use.

## 4.10 Withdrawal Management in Under-resourced Settings

Under-resourced settings, such as rural, remote, or smaller urban areas, often have fewer withdrawal management services available compared to large urban areas, particularly specialized services for specific populations (e.g., youth, pregnant individuals, older adults). In particular, rural women face the greatest number of barriers to treatment compared to urban women and rural men,<sup>377</sup> and Indigenous individuals in rural areas may face greater barriers to care compared to non-Indigenous individuals.<sup>378</sup> Furthermore, some studies report higher levels of stigma related to substance use treatment in rural populations compared to urban populations.<sup>379,380</sup>

Clinicians who practice in under-resourced areas should be aware of the range of local and referral withdrawal management services available and accessible to individuals. If inpatient withdrawal management is not locally available or accessible to individuals, outpatient care can be provided through daily clinic visits, home visits, connection to a local pharmacist, or virtual care with support from a family member or community-based support person to monitor symptoms during withdrawal and support medication adherence. If available, patients may be able to connect to clinicians who provide withdrawal management through virtual care, either via telephone or video. Clinicians can also support patients by providing or connecting patients to community-based monitoring services if available (e.g., home withdrawal program, intensive outpatient programs, community pharmacist). If inpatient services are critically needed, clinicians can make referrals to an inpatient withdrawal management service in other areas and provide support for travel if possible.

Please see [Rural and Remote Populations](#) for more information on providing AUD care to individuals in under-resourced settings.



## 4.11 Committee Consensus Recommendation –Continuity of Care

The guideline committee strongly recommends that patients who complete withdrawal management should be offered a connection to ongoing AUD care, including pharmacotherapy and psychosocial treatment, to support patient-identified treatment goals. **Withdrawal management alone is not adequate treatment for AUD, as it does not address the potentially chronic, relapsing nature of the condition.** Randomized trials and observational studies have reported that 40% to 85% of individuals with AUD resume drinking following withdrawal management, often within the first few days or weeks.<sup>381-387</sup> As a return to alcohol use is common after withdrawal management alone, it is recommended that all patients be offered ongoing care following completion of withdrawal management. Based on patient goals and available resources, withdrawal management should ideally lead to seamless engagement in ongoing pharmacotherapy, psychosocial care, or both. In circumstances in which withdrawal management alone is the only available in-person treatment (e.g., in rural, remote, or under-resourced settings), clinicians should offer withdrawal management and a referral to virtual ongoing care (e.g., virtual appointments to prescribe pharmacotherapy or to provide or refer to psychosocial treatment, including peer support groups). Most pharmacotherapy for AUD treatment is well-suited to management within the primary care setting. Pharmacotherapy initiated after withdrawal management or in consultation with an addiction specialist, can be referred to primary care for continued monitoring and prescribing.

**40% to 85% of individuals with AUD resume drinking following withdrawal management, often within the first few days or weeks**

## Recommendation 8

All patients who complete withdrawal management should be offered ongoing AUD care.

LOW Quality of Evidence

STRONG Recommendation

### Remarks

- Withdrawal management is a short-term intervention that does not resolve underlying medical, psychological, or social issues associated to AUD, and should be offered in concert with ongoing care, treatment, and support.
- The quality of evidence for this recommendation was rated as low as it is based on working group consensus, in the absence of an established body of evidence. However, studies indicate that people often return to drinking after completing withdrawal management, suggesting ongoing AUD care is needed.
- The strength of this recommendation was rated as strong based on limited evidence from randomized trials and observational studies showing high proportions of individuals with AUD resume drinking following withdrawal management, working group consensus that withdrawal management is not a standalone treatment, and the principle that ongoing AUD care is needed to help achieve patient-identified treatment goals.

# 5 Ongoing Care—Psychosocial Treatment Interventions

There is a diversity of psychosocial interventions for the treatment of AUD, ranging from structured psychotherapy to community-based supports and programs (see [Community-Based Supports and Programs](#)). Psychosocial interventions incorporate actions that target mediators (biological, behavioural, cognitive, emotional, interpersonal, social, or environmental factors) to achieve patient-directed goals.<sup>388</sup> Interventions vary based on theoretical underpinnings, duration or intensity, setting, mode of delivery, and treatment goals.<sup>389</sup> However, the importance of the therapeutic alliance is universal across psychosocial treatment interventions.<sup>388</sup> The therapeutic relationship, in which the clinician and patient work collaboratively toward the patient’s treatment goals, is predictive of positive treatment outcomes and retention in treatment.<sup>116</sup> Clinicians should develop skills such as empathic engagement, clear communication, and ability to relate to the patient to help promote a strong therapeutic relationship.

The evidence supporting psychosocial interventions is often mixed, which may be due to inconsistency in the delivery of the intervention and methodological limitations of studies examining psychosocial interventions. However, a recent study pointed to the beneficial impact of psychotherapy for AUD on incidence and progression of alcohol-associated liver disease, highlighting the importance of this treatment modality.<sup>390</sup>

## 5.1 Primary Care-led Psychosocial Treatment Interventions

Brief intervention using motivational interviewing (MI) is an evidence-based intervention that can be offered within primary care settings (see [Brief Intervention for High-Risk Drinking](#)). With training, primary care physicians, nurse practitioners, nurses, allied health professionals and other support staff can deliver MI-based counselling effectively in the primary care setting, either alone or in combination with AUD pharmacotherapy.<sup>143,391,392</sup>

Other psychosocial treatment interventions may not be easily integrated or adapted into routine primary care practice. Research is underway to evaluate and refine accessible and practice-friendly variants, including manualized family-based therapy tailored for primary care<sup>393</sup> as well as telephone, text message, and web-based mindfulness-based therapy approaches<sup>394-396</sup>; however, the efficacy and feasibility of implementing such interventions is not yet known. Recent research has demonstrated that technology-based cognitive behavioural therapy may be efficacious and feasible, which could increase accessibility outside of a specialist setting.<sup>397</sup>

## 5.2 Specialist-led Psychosocial Treatment Interventions

### In this section:

- Cognitive Behavioural Therapy
- Family-based Therapy
- Mindfulness-based Interventions
- Contingency Management
- Cognitive Bias Modification

Clinicians should provide patients with information about specialist-led psychosocial treatment interventions in the community and offer referrals to patients who express interest. Specialist-led care in this context refers to psychosocial treatment interventions that require significant training or education to deliver those interventions (e.g., cognitive behavioural therapy). In this scenario, the primary care provider should continue to play

an active role in the treatment and recovery process by connecting individuals to care and services, supporting attendance (e.g., checking in on how treatment is going and encouraging continued attendance), supporting patient-defined goals, and monitoring response to treatment. The research evidence for several specialist-led psychosocial treatment modalities—cognitive behavioural therapy, family-based therapy, mindfulness-based interventions, contingency management, and cognitive bias modification—are reviewed below. Due to the lack of research specific to AUD, studies on other substance use disorders are included in some of the evidence summaries.



**This guideline does not explicitly endorse one form of specialist-led treatment over another, as research has not consistently demonstrated that one specific approach is superior to any others. Therefore, factors such as patient and family preference, local availability, and accessibility (e.g., waitlists, out-of-pocket costs) can guide the selection and referral process.**

## 5.2.i Cognitive Behavioural Therapy

Cognitive behavioural therapy (CBT) is one form of structured, goal-directed psychotherapy. It is delivered by a trained counsellor or therapist, where patients learn how their thought processes contribute to their behaviour and emotions.<sup>398</sup> Increased cognitive awareness is combined with techniques to help patients develop new and adaptive behaviours that can alter their social environment and, in turn, reinforce change in thoughts and emotions.<sup>398</sup> Cognitive behavioural therapy for the treatment of substance use disorders is usually time-limited, consisting of approximately 10–20 one-hour sessions.<sup>398</sup>

A 2019 meta-analysis of 30 RCTs (n = 5,971; 15 trials specific to alcohol use) of CBT for adults with a substance use disorder found that CBT had significant moderate effects in terms of frequency of substance use and quantity of substance use at early and late follow-up when compared to minimal treatment.<sup>399</sup> When compared to a non-specific therapy (e.g., treatment as usual, supportive treatment, group drug counselling), CBT demonstrated similar effects, though smaller in magnitude and only at early follow-up. Effect sizes for the alcohol studies were the same as the studies of other substances.<sup>400</sup> No difference was found between CBT and other psychosocial treatments (e.g., motivational interviewing, contingency management).

### COGNITIVE BEHAVIORAL THERAPY<sup>399</sup>

STUDY		RESULTS	
Intervention	6-40 CBT sessions		<b>Frequency of substance use</b> <i>medium effect p=.09</i>
Compared to	Minimal treatment		
Study type	Meta-analysis (30 RCTs, n=5,971)		<b>Quantity of substance use</b> <i>medium effect p&lt;.001</i>

In many studies and in practice, CBT is combined with elements of other psychosocial approaches, including MI or motivational enhancement therapy (MET). A 2023 systematic review and meta-analysis (N = 19, n = 7,149) of studies of adults with


harmful alcohol use found that CBT combined with MI resulted in the greatest effect in reducing AUDIT scores (MD = -4.98 compared to no active treatment; 95% CI = -7.04 to -2.91) and was significantly better than other psychosocial interventions including BI, feedback, or a combination of those.<sup>401</sup> Furthermore, in the COMBINE study, participants were randomized to receive an intervention that combined CBT, MET, and 12-step facilitation. Psychosocial therapy showed some favourable results but not consistently across analyses. For percent days abstinent, therapy plus placebo fared better than placebo alone (80% vs. 74%;  $p = .04$ ).<sup>402</sup> However, therapy alone fared the worst in comparison (67%;  $p = .001$  compared to therapy plus placebo), indicative of a large placebo effect. When analyzing numbers of participants who were abstinent or drinking moderately with less than 3 adverse consequences from a standardized scale, collectively labeled as “good clinical outcome” in the study, psychotherapy was beneficial (71% for therapy plus placebo vs. 58% for placebo;  $p = .02$ ) and the number needed to treat was 7. These results came from the naltrexone arm of the study and were no longer significant when analysis was limited to therapy and placebo groups only. While CBT combined with MI or MET appears to be beneficial, further research is needed to delineate whether the combination is significantly different from CBT alone.

Technology-delivered CBT has been increasingly studied for use in AUD care and may be an option for people who experience barriers to receiving in-person CBT. Online lessons or modules provide patients with information on CBT strategies and may be self- or therapist-guided. A meta-analysis published in 2019 (N = 15, n = 9,838) in people with AUD or high-risk drinking levels found that technology-delivered CBT is effective in reducing alcohol consumption when used as an adjunct to treatment as usual (Hedges'  $g = .30$  [medium effect size], 95% CI: 0.10 to 0.50;  $p = .003$ ) and when compared to assessment only, waitlist, or minimal treatment (Hedges'  $g = 0.20$  [medium effect size], 95% CI: 0.022 to 0.38;  $p = .03$ ).<sup>403</sup> Conversely, there was no difference in effect between technology-delivered CBT as a stand-alone treatment compared to treatment as usual. Notably, there were no differences between technology-delivered and therapist-delivered CBT. A 2020 systematic review (N = 14) found that self-guided technology-delivered CBT—where the patient navigates through an automated program—had a significant, albeit small, effect on reducing alcohol consumption compared to receiving information about alcohol use and a waitlist control.<sup>404</sup> Therapist-guided technology-delivered CBT—where the patient receives support from a health care provider as they go through the program—was found to have small to large effect

sizes on reducing alcohol consumption compared to both a waitlist control and self-guided technology-based CBT.<sup>404</sup>

## 5.2.ii Family-Based Therapy

The defining feature of family-based therapy (FBT) for substance use disorders is that it treats individuals within the larger context of social systems where substance use may have first developed and is currently sustained. This approach has been particularly well-studied in youth populations, where social or family environments may play a significant role in the development of substance use disorders.<sup>405</sup> Social network and family-based therapies actively engage friends and family members in the treatment process and may encompass a diversity of approaches and techniques, including CBT, interpersonal therapy, communication training, and skills building. Family-based therapy is typically delivered by a trained psychologist or counsellor.

FAMILY-BASED THERAPY <sup>408</sup>	
STUDY	RESULTS
Intervention	 <b>Number of days abstinent</b> <i>medium effect p&lt;.001</i>
Compared to	
Study type	

Several systematic reviews and meta-analyses have reported that family-based approaches are efficacious for the treatment of AUD.<sup>406-408</sup> For example, a 2013 meta-analysis (N = 12, n = 1,887) of FBT among adults with substance use disorders, including AUD (8 RCTs), showed that FBT was associated with significant small to large treatment effects, with increased days abstinent or without heavy substance use following treatment (Hedges'  $g = 0.27$  [medium effect size], 95% CI: 0.13 to 0.41;  $p < .001$ ) and at short-term (Hedges'  $g = 0.46$

[medium effect size], 95% CI: 0.32 to 0.61;  $p < .001$ ) and long-term follow-up (Hedges'  $g = 0.47$  [medium effect size], 95% CI: 0.34 to 0.61;  $p < .001$ ).<sup>408</sup> These results suggest the effect of FBT is more durable over time, with lower rates of relapse to substance use or heavy substance use at 6- and 12-month follow-up compared to individualized psychosocial intervention approaches (e.g., MI, CBT, 12-step programs). Family-based therapy further demonstrated improvements in validated measures of relationship satisfaction and adjustment in comparison to those who received individually-oriented treatments (post-treatment: Hedges'  $g = 0.76$  [large effect size], 95% CI: 0.58 to 0.93;  $p < .001$ ; short-term follow-up: Hedges'  $g = 0.64$  [large effect size], 95% CI: 0.44 to 0.84;  $p < .001$ ; long-term follow-up: Hedges'  $g = 0.49$  [medium effect size], 95% CI: 0.26 to 0.72;  $p < .001$ ).<sup>408</sup> Specific to AUD, a secondary analysis of the COMBINE trial arm which randomized participants ( $n = 776$ ) to a cognitive behavioural intervention showed that involvement of a family member significantly reduced the percent of drinking days (27.58 vs. 20.75;  $p < .05$ ) at the end of the 16-week treatment.<sup>409</sup>

Unilateral family therapy, in which the partner of a non-treatment seeking individual with AUD receives therapy, is designed to increase a person's ability to effectively influence their alcohol-using partner and their relationship. A 2020 RCT ( $n = 55$ ) found that individuals with AUD whose partners participated in unilateral family therapy demonstrated significantly greater AUD treatment<sup>af</sup> initiation compared to the control group (48% vs. 15%,  $p = .038$ ), as well as improvements in the psychological health of the partner receiving unilateral therapy ( $p \leq .05$ ) and marital functioning ( $p \leq .02$ ), as demonstrated by multiple validated scales.<sup>410</sup>

Active involvement of a spouse or intimate partner in the therapy intervention has been shown to be effective for reducing drinking, drinking consequences, and relationship satisfaction. Behavioural couples therapy (BCT) is a modification to CBT that involves 12 to 20 sessions and focuses on a daily "recovery contract" to encourage abstinence, interventions to increase positive couple behaviors, and training in behavioral communication skills.<sup>411</sup> A 2008 meta-analysis of BCT for people with substance use disorders ( $N = 12$ ,  $n = 754$  couples;  $N = 8$ ,  $n = 499$  couples specific to AUD) found that BCT outperformed the active comparators

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af The type of AUD treatment (e.g., pharmacotherapy, psychosocial interventions) was not specified.



when all outcome variables and timepoints were pooled (Hedges'  $g = 0.53$  [medium-large effect], 95% CI: 0.36 to 0.70;  $p$  value not reported). When the analysis was conducted on the AUD studies, the result was similar (Hedges'  $g = 0.53$  [medium-large effect], other statistics not reported). Comparator conditions included individual CBT, 12-step facilitation, spouse-focused intervention, education, and treatment as usual. Dependent variables included frequency of use, consequences of substance use, and relationship satisfaction.<sup>406</sup> Other reviews have also indicated the efficacy of BCT in reducing substance use and improving many other outcomes, with alcohol as the focus<sup>412,413</sup> or alcohol and other substances.<sup>414,415</sup> Furthermore, an RCT comparing BCT to individual CBT in patients with AUD ( $n = 102$ ) reported that BCT resulted in greater improvements in percent days abstinent and percent of heavy drinking days during the 6 months of treatment and better drinking outcomes post-treatment.<sup>416</sup>

### 5.2.iii Mindfulness-Based Interventions

Mindfulness-based interventions (MBI) are increasingly being used in the treatment of individuals with substance use disorders, including AUD. While the MBIs described in the literature vary in terms of structure and design, they all generally share the same fundamental goals, which are achieved through individual or group practice<sup>417</sup>:



1. The development of a state of awareness characterized by full attention to internal and external experiences as they occur in any given moment.
2. The adoption of a mindset of acceptance of internal and external experiences without judgement.

In the context of substance use disorders, it has been proposed that MBI could help support individuals to learn new skills to accept or cope with stressful events. The skills developed through MBI could be used to reduce substance use behaviours that may have previously been used to suppress or avoid unpleasant emotional experiences.<sup>418,419</sup> Structured MBI programs are typically delivered by a trained psychologist or counsellor.

Systematic reviews of MBI for substance use disorders have yielded mixed results,

possibly due to inconsistency in the delivery of MBI across studies. Two systematic reviews and one meta-analysis have concluded that MBI is associated with significant reductions in substance use, including alcohol use, compared to no intervention, non-specific education programs, and active comparators (e.g., 12-step, CBT), with some studies showing additional benefits in reducing craving and stress.<sup>419-421</sup> The number of studies included in these reviews ranged from 24 to 54, and the majority were not randomized trials.<sup>419-421</sup> In contrast, a 2017 meta-analysis that included only RCTs (9 RCTs, n = 901; 7 RCTs for AUD) evaluating a standardized Mindfulness-based Relapse Prevention program<sup>422</sup> found no difference in relapse rates, frequency of substance use, retention in treatment, or depression or anxiety scores when compared to medical management alone, participation in a health education program, or other psychosocial treatment interventions (i.e., 12-step, CBT, or counselling).<sup>423</sup> The review did find a significant difference in favour of Mindfulness-based Relapse Prevention programs in terms of reducing withdrawal symptoms and craving (SMD = -0.13, 95% CI: -0.19 to -0.08), and substance-related harms (SMD = -0.23, 95% CI: -0.39 to -0.07), but the authors graded this evidence as weak.<sup>423</sup> A subsequent 2019 RCT (n = 123) that examined Mindfulness-based Relapse Prevention as an adjunct to usual care (i.e., individual or group outpatient therapy that primarily included 12-step facilitation, motivational enhancement, relapse prevention, and CBT, with participation in mutual support groups encouraged) in adults who had discontinued alcohol use in the previous 2–14 weeks showed no significant differences in alcohol consumption or the severity of alcohol-related consequences compared to usual care alone at 8 and 26 weeks post-intervention, nor were there differences in perceived stress or mindfulness scores.<sup>424,425</sup>

## MINDFULNESS-BASED RELAPSE PREVENTION<sup>423</sup>

STUDY		RESULTS	
Intervention	Mindfulness-based relapse prevention, 8 x 2-hr sessions	 <b>Frequency of substance use</b> (no change)	
Compared to	Treatment as usual or other therapy	 <b>Quantity of substance use</b> (no change)	
Study type	Meta-analysis (9 RCTs, n=901)		

Overall, the evidence base for MBI is limited due to a relatively small number of randomized trials with small sample sizes and heterogeneity in the study methodology and outcomes assessed. More rigorous randomized controlled trials are needed before a definitive conclusion can be drawn with regards to the effects of MBI on alcohol-related outcomes.

## 5.2.iv Contingency Management

Contingency management (CM) is a well-studied approach for improving outcomes of substance use disorder treatment.<sup>426-428</sup> Contingency management uses positive reinforcement to encourage behavioural change; most often, financial incentives or vouchers are provided when an individual achieves specific goals as outlined in their treatment plan. Typically, treatment goals are abstinence-based, and positive or negative consequences are based on objective evidence of recent substance use (e.g., urine drug testing). However, behavioural markers can also be used (e.g., adherence to medication, clinic attendance, participation in peer support groups). Contingency management is not a standalone treatment for substance use disorders and is always delivered as part of a more comprehensive treatment plan.

Although a number of RCTs have found that CM is effective in improving treatment outcomes for other substance use disorders,<sup>426,429</sup> its usefulness for AUD has been limited by the technology available to test for and monitor alcohol use. Contingency management has demonstrated efficacy and feasibility for AUD in a limited number of RCTs. A 2013 RCT (n = 30)<sup>430</sup> and 2018 RCT (n = 40)<sup>431</sup> found participants in the contingent group had more negative breathalyzer results (mean = 87.1% vs. 66.9%,  $p \leq .001$ ),<sup>430</sup> increased rates and durations of alcohol abstinence (mean percent days abstinent: 85% vs. 38%,  $p < .001$ ; longest duration of negative samples: 16.8 vs. 5.9 days,  $p \leq .001$ ),<sup>430,431</sup> and decreased drinking days ( $p < .04$ )<sup>430,431</sup> compared to those in the control group. In both studies, a combination of breathalyzers and cell phone or remote monitoring were used, with participants rating the intervention highly in terms of satisfaction, effectiveness, and ease of use.<sup>431</sup> The majority of breathalyzer test results were returned on time, regardless of treatment group, supporting the feasibility of incorporating technology-based CM into AUD treatment, where such resources are available.<sup>430,431</sup>

Contingency management has had relatively poor uptake in practice, due to a variety of barriers including philosophical objections, costs (vouchers, biological testing, staff training and time),<sup>432-434</sup> lack of infrastructure and resources, time commitment (for patients and providers), and lack of knowledge and training,<sup>434-436</sup> making it inaccessible for many individuals with AUD. Clinicians should ensure their patients understand the components of CM before offering a referral, as the use of financial incentives may not align with patient goals and preferences. Furthermore, CM may be more appropriate for patients who have a self-identified treatment goal of abstinence, as CM tends to reinforce behaviour based on objective measures of alcohol use (e.g., urine drug testing) rather than self-reported reductions in alcohol use. More research is needed to determine whether CM is an effective and feasible strategy for the management of AUD in “real-world” clinical care settings.

## 5.2.v Cognitive Bias Modification

Cognitive bias modification (CBM) is a family of interventions that target substance-related cognitive biases. The intervention includes training paradigms<sup>ag</sup> that address attentional, behavioural, or evaluative cognitive processes that are triggered by substance use-related environmental cues (i.e., cognitive biases) that help to maintain substance use disorder-related behaviours.<sup>437</sup> In the context of high-risk alcohol consumption and AUD, individuals who consume alcohol have been found to more frequently respond with or to alcohol-related cues rather than non-alcohol-related cues.<sup>438</sup>

Meta-analyses investigating the effects of CBM for AUD have found small to non-significant results. A 2019 meta-analysis (N = 14, n = 2,435) examining CBM as a behaviour change intervention for alcohol and tobacco use disorders using individual patient data found CBM had a small beneficial effect on both cognitive bias (posterior mean = 0.23, 95% credible interval: 0.06 to 0.41) and relapse rates

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ag Briefly, training paradigms for CBM involve speeded reaction-time tasks in which individuals have to react to alcohol-related and non-alcohol-related stimuli with some form of stimulus-response contingency. Cognitive bias modification training uses the stimulus-response contingency to create a new stimulus-response to alcohol-related cues.<sup>437</sup>

(posterior mean = -0.27, 95% credible interval: -0.68 to 0.22), but did not have an effect on reduction of substance use.<sup>437</sup> A meta-analysis published in 2016 that included RCTs of both alcohol and tobacco use disorder (N = 25, 18 AUD RCTs, n = 3,175) found mixed effects of CBM. Cognitive bias modification had no significant effect on addiction outcomes and craving post-treatment; however, there was a small, significant effect on cognitive bias (Hedges'  $g = .60$  [large effect size], 95% CI: 0.39 to 0.79). At follow-up, CBM had a significant effect for alcohol-related addiction outcomes (Hedges'  $g = .18$  [small effect size], 95% CI: 0.03 to 0.33).<sup>439</sup> Conversely, a 2018 analysis found differing results when studies included in the 2016 meta-analysis were differentiated by study type, mode of delivery, and population.<sup>440</sup> In this analysis, CBM had small but robust effects on treatment outcomes when administered as an adjunct treatment in clinical settings for individuals with AUD, and clinically relevant effects on reduced drinking in individuals with high-risk alcohol consumption. The review authors suggest CBM has potential as an adjunct treatment, specifically when integrated with CBT, and could be offered as a technology-based intervention. Further research into CBM is needed, particularly studies that aim to establish clinical efficacy as opposed to proof-of-concept studies, as researchers suggest there is not yet enough evidence either in support of or against CBM for AUD.<sup>437</sup>

## 5.2.vi Psychosocial Treatment Interventions and Concurrent Mental Health Disorders

Assessment, treatment, and monitoring of emotional and mental health is an essential component in caring for patients with AUD, especially given the high prevalence of concurrent mental health diagnoses in this population (e.g., post-traumatic stress disorder [PTSD], depression, anxiety).<sup>73,441</sup> Histories and ongoing experiences of trauma are common among people with substance use disorders, and AUD is particularly prevalent among people with PTSD.<sup>442,443</sup> Despite a limited number of controlled trials, there is some evidence that the inclusion of specialist-led psychosocial treatment interventions can improve both substance use and mental health outcomes for individuals with substance use disorders and concurrent mental health disorders, including anxiety and depression,<sup>444,445</sup> PTSD,<sup>442,446</sup> and severe mental illness (e.g., schizophrenia, schizoaffective disorder, bipolar disorder).<sup>447</sup> Individuals with known post-traumatic symptomology should be offered referral to a trauma specialist where possible. Please see [Trauma- and](#)

[Violence-Informed Practice](#) for more information on providing trauma-informed care. Preliminary evidence from a 2018 RCT (n = 228) suggests individuals with severe AUD or high levels of depression, in particular, may benefit from specialist care.<sup>448</sup> However, it is noted that the evidence for psychosocial and medication treatment efficacy in this patient population tends to be of lower quality, and the effect sizes calculated in meta-analyses were generally small to moderate in scale.<sup>449</sup> In addition, there is a lack of evidence for determining whether simultaneous, integrated, or sequential interventions for AUD and the mental health condition would be most effective.

Clinicians should be aware of the connection between socially constructed factors (e.g., poverty, systemic racism, and housing insecurity) and mental health; the impacts of colonization and systemic oppression on both substance use and concurrent mental health disorders; as well as the links between trauma and substance use and mental health disorders. Treatment plans should be developed with awareness of these factors and aim to mitigate them where possible.

## 5.2.vii Psychosocial Treatment Interventions in Youth

A 2010 meta-analysis (16 RCTs, n = 2,154) evaluating various individual (e.g., MI, CBT, 12-step approach) and family-based psychosocial treatment interventions for AUD in patients aged 12–19, found a significant medium sized effect on pooled alcohol consumption treatment outcomes (Hedges'  $g = -.62$  [large effect size], 95% CI, -0.83 to -0.40;  $p < .001$ ) across studies.<sup>450</sup> Individual psychosocial treatments demonstrated a larger effect size (Hedges'  $g = -.75$  [large effect size], 95% CI: -1.10 to -0.40;  $p < .001$ ) compared to family-based interventions (Hedges'  $g = -.46$  [medium effect size], 95% CI: -0.66 to -0.38;  $p < .001$ ). However, effect sizes decreased with length of follow-up, with larger effect sizes shown when follow-up was at 6 months or less (Hedges'  $g = -.66$  [large effect size], 95% CI: -0.95 to -0.38;  $p < .001$ ) compared to when follow-up was more than 6 months (Hedges'  $g = -.50$  [large effect size], 95% CI: -0.68 to -0.32;  $p > .001$ ).

Three meta-analyses and one review assessing psychosocial interventions in youth with substance use disorders, including AUD, have shown that the effects of FBT on engagement and retention in treatment, reduction in alcohol and drug use, sustained abstinence, and improved psychological, social, and family functioning are

comparable to those of CBT and superior to those of other psychosocial treatment interventions.<sup>450-453</sup> As with adult populations, effect sizes tended to diminish over time; however, a limited number of clinical trials that incorporated long-term follow-up have reported that treatment effects of FBT remain significant relative to comparator groups at 12 or more months post- intervention.<sup>393</sup>

Strong therapeutic alliances with both youth and their family members are predictive of patient success in FBT.<sup>393,454</sup> Family involvement in the treatment of youth should be actively encouraged, if appropriate, and family members should be supported with sufficient information and training. However, not all youth have healthy or positive relationships with their family members and decisions to include family members should be guided by an understanding of the family dynamic and the patient's wishes. See [Family and Social Circle Involvement in Care](#) for more information.

## 5.2.viii Psychosocial Treatment Interventions in Pregnant Individuals

There is limited evidence regarding the effectiveness of psychosocial treatment interventions for the treatment of AUD in pregnant individuals. A 2009 systematic review of psychological and educational interventions for reducing alcohol use in pregnancy (4 RCTs, n = 715) concluded that overall, there is insufficient data on their effectiveness in reducing alcohol consumption or supporting abstinence, with limiting factors including inconsistent results, small sample sizes, high risk of bias, and heterogeneity in intervention types and outcomes assessed across trials.<sup>234</sup> Nonetheless, although the evidence base is sparse, due to the known maternal/parental and fetal risks of alcohol use in pregnancy, most clinical practice guidelines do recommend that pregnant individuals with AUD be offered psychosocial treatment interventions to support abstinence or reduced alcohol consumption.<sup>185,371</sup> Due to historical and current discrimination and stigma, treatment approaches for Indigenous pregnant patients must be handled with great sensitivity and safety. Guidance and strategies to support culturally safe care can be found in the Society of Obstetricians and Gynaecologists of Canada [Consensus Guideline for Health Professionals Working With First Nations, Inuit, and Métis](#)<sup>183</sup> and in its [Companion Piece](#).

## 5.2.ix Psychosocial Treatment Interventions in Older Adults

Limited studies of psychosocial treatment interventions for the treatment of AUD in older adults have been published. There are a small number of studies supporting the use of CBT for older adults, with results suggesting CBT is effective in this population in terms of promoting higher abstinence rates from substance use compared to participants who dropped out of treatment<sup>455</sup> and higher percentage of days abstinent and reducing heavy drinking days compared to vocational enhancement.<sup>456</sup> Cognitive behavioural therapy may be more useful for older adults when clinicians support the patient to remember the information and skills learned by summarizing and repeating information, encouraging the patient to take notes, and providing handouts, forms, or reminders to the patient.<sup>457</sup> Older adults may express preference for age-specific psychosocial treatment interventions, as opposed to mixed-age treatment interventions, particularly older adults who may have more comorbidities and functional limitations.<sup>458</sup> Clinicians should provide or offer referrals to age-specific psychosocial treatments when appropriate and available.

In 2019, the Canadian Coalition for Seniors' Mental Health published [Canadian Guidelines on Alcohol Use Disorder Among Older Adults](#). Their recommendation suggests routinely offering psychosocial treatment interventions to older adults, including in combination with pharmacotherapy interventions.

## 5.2.x Duration of Treatment

There is a lack of research evidence to guide the optimal duration of psychosocial treatment interventions for AUD. A 2018 meta-analysis of 48 studies (n = 8,984) of outpatient psychosocial treatment interventions for AUD found that neither planned nor completed treatment duration (i.e., attendance in weeks, duration of sessions, or frequency of sessions per week) were associated with improved long-term outcomes of individuals with AUD.<sup>459</sup> Additionally, other factors, such as an individual patient's needs, circumstances, and preferences, as well as access to and availability of specialists, programs, and services in a particular community, often determine intensity and duration of psychosocial treatment interventions. As such, there is insufficient evidence to make recommendations on the optimal duration of psychosocial treatment interventions. However, it is emphasized that primary care



providers can play a critical role in ensuring patients are supported during transitions in care and after specialist-led psychosocial treatment has concluded.

### 5.2.xi Accessibility and Other Considerations

Important considerations when discussing options for referral to specialist-led psychosocial treatment services are that publicly-funded programs often have waiting lists, and the costs of private counsellors or facilities (i.e., non-publicly funded programs) may not be covered by provincial and territorial health insurance or extended health insurance plans, necessitating out-of-pocket payment. Clinicians should ask patients if they have non-insured health benefits (NIHB) or extended health insurance that covers specialized psychosocial treatment, as this may alleviate some financial burden for patients who seek care from private counsellors or services. In rural and remote areas, referral to specialized treatment programs may also require patients to travel long distances or leave their communities in order to access care, which may not be feasible or practical for some individuals. Please see [Individuals Experiencing Homelessness](#) for information on providing and reducing barriers to care for people experiencing homelessness. Again, it is emphasized that a lack of access or a patient's decision not to participate in specialized psychosocial treatment should not be a barrier to accessing evidence-based pharmacotherapy and related services in primary and other care settings; likewise, a patient's decision to not receive pharmacotherapy should not be a barrier to receiving a referral to psychosocial intervention for AUD.

### 5.2.xii Section Summary and Recommendation

This guideline recommends that clinicians should provide patients with information about specialist-led psychosocial treatment interventions in the community and offer referrals to patients who express interest. A lack of access to or a patient's decision not to participate in specialized psychosocial treatment should not be a barrier to accessing evidence-based pharmacotherapy and related services in primary care; likewise, a patient's decision to not receive pharmacotherapy should not be a barrier to receiving a referral to psychosocial intervention for AUD. If specialist-led treatment is not available, clinicians should advocate for expansion of specialist-led treatments, and provide other psychosocial and pharmacological AUD treatment options when indicated.

The recommendations for specialist-led psychosocial treatments are based on best available evidence and committee consensus. Several reviews and subsequent RCTs have found that CBT is associated with small to moderate, but significant, reductions in likelihood of relapse and alcohol consumption in both youth<sup>451</sup> and adults.<sup>460</sup> Family-based therapies have also been associated with small but significant beneficial effects on alcohol and other substance use outcomes, as well as improvements in relationship satisfaction and adjustment in both adults<sup>406-408</sup> and youth.<sup>450-453</sup> There is limited and mixed evidence regarding the efficacy of mindfulness-based interventions in the treatment of AUD. More research is needed to clarify the role of these therapeutic approaches within the AUD continuum of care in order to make explicit recommendations. There is insufficient evidence to recommend routine use of contingency management (CM) approaches in the primary care management of AUD, and a need for further research to develop practice-friendly variants of CM that would be feasible in primary care settings.

## Recommendation 9

**Adults and youth with mild to severe AUD should be offered information about and referrals to specialist-led psychosocial treatment interventions in the community.**

MODERATE Quality of Evidence

STRONG Recommendation

### Remarks

- The referring clinician should continue to play an active role after connecting individuals to psychosocial treatment interventions by checking in with patients on their experience and overall satisfaction, encouraging regular attendance, and including patient-defined goals in their treatment plan.
- Referring clinicians should establish regular communication with specialist providers and programs to facilitate continuity of care, transitions in care, and to share relevant information (with the patient's permission; e.g., assessments, progress notes, discharge summaries).
- Selection of a psychosocial intervention should be based on patient preference and needs, as research has not consistently demonstrated the superiority of any specific approach. Examples of possible approaches include cognitive behavioural therapy, family-based therapy, and mindfulness-based therapy.
- The quality of evidence for this recommendation was rated as moderate based on several meta-analyses and RCTs that have demonstrated psychosocial treatment interventions result in small to moderate treatment effects on various alcohol outcomes.
- The strength of this recommendation was rated as strong based on the quality of evidence, working group consensus, the effectiveness of psychosocial treatment interventions, and the benefits of psychosocial interventions relative to the potential risks.

# 6 Ongoing Care—Pharmacotherapy

## In this section:

- Naltrexone
- Acamprosate
- Topiramate
- Gabapentin
- Disulfiram
- Baclofen
- Ondansetron

Pharmacotherapy can play an important role in assisting individuals with AUD to reduce or stop drinking, yet is underutilized in the management of AUD.<sup>461</sup> For example, only 1.3% of individuals diagnosed with AUD in Manitoba between 1996 and 2015 were prescribed AUD pharmacotherapy.<sup>34</sup> Primary care providers' lack of education, knowledge, and training are consistently identified as barriers to prescribing AUD pharmacotherapy.<sup>39,462,463</sup> However, research has shown that when these practitioners are provided with evidence-based clinical care guidance and practice tools, they can effectively prescribe these medications in alignment with their patients' goals, leading to clinically meaningful improvements in treatment outcomes.<sup>25,464</sup> Indeed, a recent study pointed to the health benefits of AUD pharmacotherapy treatment on incidence and progression of alcohol-associated liver disease, highlighting the importance of this treatment modality.<sup>465</sup> Conversely, research has also demonstrated that certain ineffective and potentially harmful medications can be over-prescribed to persons with AUD resulting in avoidable health care system costs and potential worsening of AUD outcomes.<sup>466-468</sup>

**This guideline recommends that patients with moderate to severe AUD should be offered evidence-based pharmacotherapy for AUD in primary care settings.**

Additionally, regardless of AUD severity, any patient who has stopped or reduced their drinking but continues to experience strong alcohol cravings or is at risk of return to drinking (“relapse”) may be an appropriate candidate for evidence-based pharmacotherapy. Clinicians should discuss the risks and benefits of all treatment modalities and offer evidence-based pharmacotherapy for AUD in conjunction with psychosocial interventions (see [Ongoing Care—Psychosocial Treatment Interventions](#)), as appropriate to support patient goals and preferences. For patients using multiple substances, treatment may provide benefit to both alcohol and other substance use (see [Co-occurring Substance Use Disorders](#)).

## 6.1 Setting Patient-Centred Treatment Goals

Traditionally, abstinence or cessation of alcohol use has been viewed as the primary goal of AUD treatment. While abstinence may result in better outcomes and many individuals identify it as a treatment goal, it is also important to recognize that not all individuals with AUD view abstinence as an acceptable, desirable, or realistic treatment goal.<sup>469</sup> In this context, expectations of abstinence as a treatment goal may prevent some individuals from seeking treatment for AUD or act as a barrier to continued engagement in care.<sup>470</sup> In recent years, alongside approaches that promote abstinence, there has been increased recognition that a reduction in drinking may be a valid and important treatment goal for some individuals.<sup>63</sup> Studies have shown that individuals with AUD are more likely to achieve self-identified treatment goals, whether that is a reduction in drinking or abstinence, than goals that are set for them that may be inconsistent with their own current treatment goals.<sup>471,472</sup>

**Not all individuals with AUD view abstinence as an acceptable, desirable, or realistic treatment goal . . . a reduction in drinking may be a valid and important treatment goal for some individuals.**

Abstinence remains the safest treatment goal for patients, as there is no agreed-upon safe level of alcohol consumption.<sup>469</sup> Research indicates that individuals with a treatment goal of abstinence may differ from those with a non-abstinence goal. Individuals with a goal of abstinence are more likely to have severe AUD, more alcohol-related problems, more concurrent physical and mental health conditions, less social support, and higher confidence in their ability to remain abstinent from alcohol use.<sup>473</sup> Studies suggest that individuals with a treatment goal of abstinence report better alcohol use outcomes compared to those with a non-abstinence goal, including outcomes related to days abstinent,<sup>474-477</sup> heavy alcohol consumption,<sup>477,478</sup> and return to alcohol use.<sup>475</sup> In contrast, a non-abstinent treatment goal can lead to greater reductions in heavy drinking during pharmacotherapy treatment.<sup>479</sup> A 2020 meta-analysis (N = 22, n = 4,204) found that among individuals with AUD who were allowed to choose their own treatment goal, those with a goal of abstinence were more likely to achieve low-risk drinking compared to those with a non-abstinence goal (OR: 0.60, 95% CI: 0.40 to 0.90); however, if goal-specific treatment was provided (i.e., treatment tailored to support either an abstinence or non-abstinence goal), there was no difference in low-risk drinking between groups.<sup>480</sup>

As an emerging area of research, a growing number of RCTs have examined a reduction in alcohol consumption as a treatment goal, as opposed to previous studies that have focused solely on abstinence as a treatment goal.<sup>481</sup> There is promising evidence that reducing alcohol consumption is associated with health benefits.<sup>110,482,483</sup> A 2013 meta-analysis (N = 16, n = 4,951) demonstrated that reduced alcohol consumption is associated with a reduction in mortality compared to continued heavy alcohol use.<sup>31</sup> Another study, published in 2021, re-analyzed data from 2 RCTs,<sup>402,484</sup> (n = 1,500) and showed that reduced drinking was associated with significantly better mental health and quality of life and fewer adverse drinking-related consequences 3 years post-treatment when compared to no change in or increased alcohol consumption.<sup>483</sup> Although there is a lack of RCT data showing improved physical health outcomes, findings from a number of large observational cohort studies and one meta-analysis do show that reductions in alcohol consumption are associated with reductions in alcohol-attributable morbidity and mortality.<sup>109,110,124,138,483,485,486</sup>




While acknowledging that there are limitations to the evidence base, it is the consensus of this committee that clinicians should inform all patients of the health and social risks of excessive alcohol use and adopt a treatment approach that supports individual patient autonomy in selecting from a spectrum of goals, including safer alcohol consumption, reduced alcohol consumption, and abstinence. The committee recognizes that, alongside models that focus on abstinence, models that focus on a reduction in drinking and alcohol-related harms are useful and important for some patients helping them achieve their own treatment goals. For some, initial reductions in use may be followed by later abstinence. This patient-centred approach may also support continued engagement in care among individuals who return to alcohol use.

## 6.2 First-line Pharmacotherapies

### 6.2.i Naltrexone

Naltrexone is a mu-opioid receptor antagonist<sup>ah</sup> that has been shown to block euphoria associated with alcohol consumption.<sup>488</sup> It is hypothesized to work by diminishing the rewarding effect of alcohol in the brain following its consumption, as well as reducing cravings for alcohol in some individuals.<sup>488</sup> This diminishing effect on neural reward pathways is consistent with research findings that naltrexone is particularly effective in preventing a return to heavy drinking following a temporary return to alcohol use.

Naltrexone has a well-established evidence base for safety and efficacy in the treatment of AUD.<sup>261,479,487</sup> A 2010 Cochrane review and meta-analysis of 50 RCTs (n = 7,793) reported that participants treated with naltrexone had a 17% lower likelihood of engaging in heavy drinking (risk ratio [RR]: 0.83, 95% CI: 0.76 to 0.90), and had 4% fewer drinking days per month (mean difference [MD] = -3.89, 95% CI: -5.75 to -2.04) than those who received placebo.<sup>487</sup> Naltrexone-treated participants also showed a greater reduction in heavy drinking days (MD = -3.25, 95% CI: -5.51 to -0.99) and in the amount of alcohol consumed (MD = -10.83 grams, 95% CI: -19.69 to -1.97) compared to the placebo group.<sup>487</sup> A 2013 meta-analysis (N = 45, n = 5,434)

NALTREXONE <sup>479</sup>		
STUDY	RESULTS	
Intervention	50 mg naltrexone for 3 months	 <b>Abstinence</b> small effect p=.001
Compared to	Placebo	 <b>Heavy drinking</b> small effect p<.001
Study type	Meta-analysis (45 RCTs, n=5,434)	 <b>Craving</b> small effect p=.005

ah Nalmefene is an opioid antagonist with potentially similar effectiveness to naltrexone<sup>487</sup> that is used for the management of AUD in some countries; however, it is not approved by Health Canada for any use.

further demonstrated naltrexone had a significant positive effect on abstinence outcomes (Hedges'  $g = 0.116$  [small effect size], 95% CI: 0.049 to 0.183;  $p = .001$ ), heavy drinking outcomes (Hedges'  $g = 0.189$  [small effect size], 95% CI: 0.123 to 0.255;  $p < .001$ ), and craving (Hedges'  $g = 0.144$  [small effect size], 95% CI: 0.045 to 0.244;  $p = .005$ ).<sup>479</sup> While most systematic reviews and meta-analyses have found positive effects of naltrexone for reducing alcohol consumption, there have been mixed results in terms of maintaining abstinence. For example, a 2020 network meta-analysis ( $N = 64$ ; naltrexone-specific studies:  $N = 17$ ,  $n = 878$ ) found that, compared to placebo, naltrexone reduced the odds of treatment dropout (odds ratio [OR] = 0.70, 95% CI: 0.50 to 0.98) but had no effect on maintaining abstinence for up to 12 months.<sup>489</sup>

Naltrexone is contraindicated in individuals with acute hepatitis and liver failure, and although it no longer carries a “black box warning” for hepatotoxicity,<sup>490</sup> caution and increased monitoring are advised if prescribed to patients with hepatic impairment. Naltrexone may also be contraindicated in patients currently taking prescribed or illicit opioids, as it will initiate precipitated withdrawal in individuals who have not ceased opioid use for 7–10 days<sup>ai</sup>.<sup>492</sup> Commonly reported side effects in placebo-controlled trials of naltrexone include somnolence (29.5% in the naltrexone-treated group vs. 17.8% in the placebo group), nausea (25.8% vs. 16.3%), vomiting (16.9% vs. 10.4%), decreased appetite (17.7% vs. 11.8%), abdominal pain (15.9% vs. 7.5%), insomnia (16.4% vs. 13.4%), and dizziness (11.9% vs. 6.2%).<sup>487</sup>

A period of 3–7 days of abstinence or completion withdrawal management prior to starting naltrexone or a treatment goal of non-abstinence were all predictive of greater benefits on heavy drinking.<sup>479</sup> Additional research suggests that predictors of a positive response to naltrexone include high levels of craving and a family history<sup>aj</sup> of AUD.<sup>495,496</sup> Two recent RCTs published in 2017 ( $n = 152$ ) and 2018 ( $n = 146$ ) have also reported that naltrexone may be more effective in individuals with

- 
- ai Naltrexone may have a protective effect against overdose for individuals who regularly use alcohol and infrequently use opioids and may reduce opioid use.<sup>491</sup> Different opioids (illicit or prescribed) have varying half-lives and clinicians should be mindful of how long it would take to clear from the patient's system when making an informed decision about when it would be safe to start naltrexone. Subcutaneous injectable extended-release buprenorphine may remain in the body for over a month, even after cessation of the injection series. Naltrexone is to be cautiously used due to potential risk of precipitated withdrawal.
- aj Individuals who have a first-degree relative with AUD may respond better to naltrexone compared to those without a first-degree relative with AUD; however, evidence regarding this association is mixed.<sup>494</sup>

AUD who smoke tobacco or use electronic cigarettes, but these results have yet to be validated in large prospective trials.<sup>497,498</sup> As would be expected, treatment adherence is also highly correlated with positive treatment outcomes. Medical management increases the likelihood of high treatment adherence, which has been shown to increase days abstinent and the time to first heavy drinking day and decrease heavy drinking days. Clinicians should routinely check-in and provide support with medication adherence when needed, as well as other patient-defined treatment goals, through medical management and regular follow-up visits.<sup>487,499,500</sup> See [Appendix 5: AUD Pharmacotherapy](#) for further prescribing information about naltrexone, including contraindications and cautions.

### 6.2.i.1 Targeted or “As-Needed” Naltrexone Dosing

In the majority of clinical trials, naltrexone has been studied as a dose taken once daily. However, several studies have found that when taken “as needed” (e.g., prior to drinking or when significant cravings are experienced), “targeted” naltrexone can reduce alcohol consumption in individuals who meet criteria for high-risk drinking, including those diagnosed with mild to severe AUD.<sup>262,501-503</sup> Compared to placebo, targeted naltrexone may reduce drinks per drinking day (19% less,  $p = .014$ )<sup>502</sup> and increase the likelihood of maintaining a reduction in drinking following continuous treatment ( $p = .05$ ).<sup>262</sup> Reported effect sizes on alcohol-related outcomes were small to moderate,<sup>504</sup> which is consistent with published treatment effects of daily-dosed naltrexone.<sup>261,487</sup> Taken together, these results suggest that targeted naltrexone is an effective approach for reducing alcohol consumption and alcohol-related harms.<sup>504</sup> Targeted dosing regimens may be preferred for patients who experience challenges with adherence or significant side effects with daily-dosed regimens, patients who binge-drink alcohol, or patients who engage in high-risk drinking but do not meet the criteria for an AUD. For patients who have responded well to naltrexone and express interest in reducing their medication burden, prescribing naltrexone “as-needed” may have advantages in supporting these patients to maintain their goals and reduce daily dosing, rather than discontinuing pharmacotherapy.




### 6.2.ii Acamprosate

Acamprosate’s mechanism of action is not well understood, but it is thought to modulate glutamate-mediated excitation through interaction with calcium channels



and to indirectly affect GABA-mediated inhibition of neural activity, which becomes imbalanced by chronic alcohol consumption.<sup>505</sup> Generally, acamprosate reduces general neuronal hyperexcitability and leads to the subjective effects of diminished arousal, anxiety, and insomnia. These effects are believed to reduce symptoms associated with withdrawal from alcohol and prolong abstinence.

Acamprosate has an established evidence base for safety and efficacy in the treatment of AUD.<sup>479,493,506-509</sup> A 2010 Cochrane review and meta-analysis of 24 RCTs (n = 6,915) found that acamprosate significantly reduced the likelihood of a return to any drinking by 14% (RR = 0.86, 95% CI: 0.81 to 0.91) and increased the cumulative duration of abstinence by 11 days (95% CI: 5.08 to 16.81) compared to placebo.<sup>493</sup> In addition, the review showed that the effects of acamprosate persisted for 3–12 months after treatment discontinuation.<sup>493</sup> A subsequent 2013 meta-analysis (N = 16 RCTs, n = 4,349) found similar results with acamprosate significantly improving abstinence outcomes at end of treatment (Hedges' g = 0.359 [medium effect size], 95% CI: 0.246 to 0.472; p < .001) and at several time points following treatment, compared to placebo.<sup>479</sup> Acamprosate did not reduce heavy drinking or craving. Further, a 2020 meta-analysis (N = 64) found that, compared to placebo, acamprosate increased the odds of maintaining abstinence up to 12 months (OR = 1.86, 95% CI: 1.49 to 2.33) and reduced treatment dropout (OR = 0.73, 95% CI: 0.62 to 0.86).<sup>489</sup>

ACAMPROSATE <sup>479</sup>	
STUDY	RESULTS
<b>Intervention</b>	1,998 mg or 1,332 mg acamprosate for 6 months
<b>Compared to</b>	Placebo
<b>Study type</b>	Meta-analysis (16 RCTs, n=4,349)
	 <b>Abstinence</b> medium effect p<.001  <b>Heavy drinking</b> no effect  <b>Craving</b> no effect

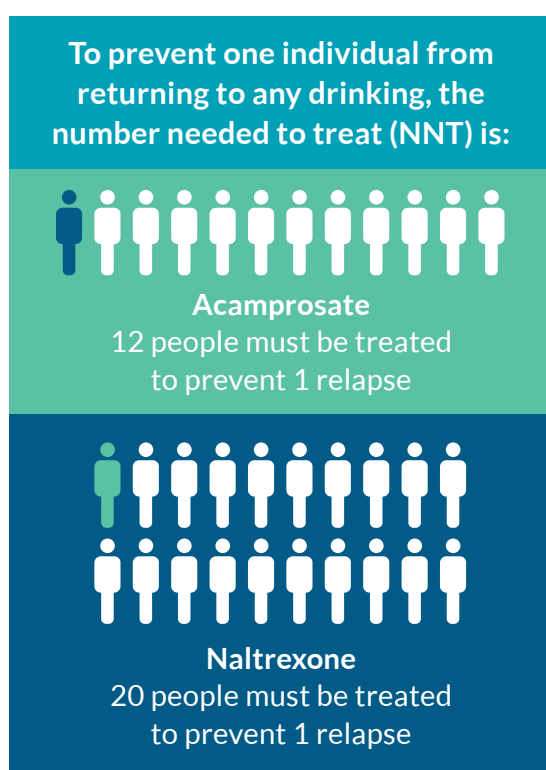
The majority of clinical trials of acamprosate have taken place in Europe, where it was used for several decades to treat AUD prior to its approval in North America. This has raised some concerns that research findings may not be generalizable to North American settings, particularly as a large 2006 U.S. trial (n = 1,383) showed that acamprosate was no more effective than placebo at reducing alcohol consumption.<sup>402</sup> This finding is contrary to most European acamprosate trials, which have found acamprosate is effective in reducing relapse rates and increasing abstinence rates.<sup>510-512</sup> A 2015 meta-analysis (49 RCTs, n = 9,435) compared acamprosate and naltrexone treatment trials conducted in Europe to trials conducted in non-European countries and concluded that, overall, trial location did not appear to influence abstinence or relapse rates for acamprosate, but that treatment discontinuation and participant characteristics did differ by location.<sup>513</sup> Participants in European trials were more likely to have completed withdrawal management prior to the trial, have a treatment goal of abstinence, have a longer treatment duration, and be recruited via treatment services than non-European study participants. The review authors speculated that European participants may, therefore, be more engaged with treatment services prior to starting medication compared to those outside of Europe who were more likely to be entering treatment at the start of the trial, which could account for observed differences in treatment discontinuation.<sup>513</sup> No interaction was observed between drop-out and trial location for naltrexone trials. Overall, the review concluded that, based on available evidence, acamprosate is effective for the treatment of AUD, but suggested that an individual patient's treatment goal is an important factor to consider when selecting a first-line treatment (see [Selecting Between Naltrexone and Acamprosate](#)).<sup>513</sup>

Acamprosate is generally well tolerated, and the most common side effects are gastrointestinal disturbances (e.g., diarrhea, nausea, vomiting). In RCTs, diarrhea is the only side effect reported more frequently for acamprosate than placebo.<sup>493</sup> Although this side effect can occur in up to 16% of patients, it usually resolves quickly within a few days.<sup>392</sup>

Clinical trials show that being abstinent or completing withdrawal management prior to starting treatment; having abstinence as a treatment goal; or adjusting dosage based on the patient's weight result in increased treatment efficacy for acamprosate.<sup>260,479,514</sup> Motivation and treatment readiness may be particularly important factors for adherence, as due to its low bioavailability, acamprosate must be administered at a dosage of nearly 2g split into 3 doses per day. Providing

encouragement and informal counselling to support patients with medication adherence is critical at treatment onset and on an ongoing basis.<sup>514</sup> Additional predictors of treatment success with acamprosate that have been identified in the literature include higher baseline anxiety levels, a physiological dependence on alcohol, a lack of family history of AUD, and a later age of AUD onset (i.e., > 40 years of age).<sup>515</sup> See [Appendix 5: AUD Pharmacotherapy](#) for further prescribing information, including contraindications and cautions.

### 6.2.iii Selecting Between Naltrexone and Acamprosate



A 2014 meta-analysis (N = 123 [122 RCTs, 1 cohort], n = 22,803; acamprosate: 27 RCTs, n = 7,519, naltrexone: 53 RCTs, n = 9,140) of outpatient pharmacotherapy for adults with AUD found that both acamprosate (risk difference (RD) = -0.09, 95% CI: -0.14 to -0.04) and naltrexone (RD = -0.05, 95% CI: -0.10 to -0.002) were associated with a lower likelihood of return to alcohol use than placebo.<sup>261</sup> When directly compared with one another (4 RCTs, n = 1,141), no significant differences were found between acamprosate and naltrexone in alcohol consumption outcomes.<sup>261</sup>

While the overall superiority of one medication over the other has not been established conclusively, there is evidence that naltrexone may be more effective in reducing heavy drinking, while acamprosate may be more effective in supporting abstinence from alcohol. The aforementioned 2014 meta-analysis calculated that to prevent one individual from returning to any drinking, the number needed to treat (NNT) was 20 (95% CI: 11 to 500) for naltrexone, and 12 (95% CI: 8 to 26) for acamprosate.<sup>261</sup> To prevent return to heavy drinking, the NNT

for naltrexone was calculated to be 12 (95% CI: 8 to 26) whereas acamprosate was not significantly better than placebo.<sup>261</sup> Three independent meta-analyses, one published in 2008 (N = 41, n = 5,280), one in 2012 (N = 64, n = 10,993), and one in 2020 (N = 64, acamprosate: N = 18, n = 2,286) have reached similar conclusions:

**Acamprosate may be more effective for patients with a goal of abstinence, whereas naltrexone may be beneficial for patients with a goal of reduced drinking or abstinence.<sup>479,489,516</sup> Thus, a patient's treatment goals are a key consideration when selecting between these medications.**

A patient's family history of AUD may also be a consideration. There is some evidence to suggest that individuals with a family history of AUD have better outcomes with naltrexone,<sup>494</sup> while individuals without a family history of AUD may have better outcomes with acamprosate.<sup>515</sup> Additional information to consider when selecting between these two medications is summarized in [Appendix 5: AUD Pharmacotherapy](#).

#### 6.2.iii.1 Coverage

Naltrexone and acamprosate are included in provincial and territorial formularies across Canada. Clinicians should confirm type of coverage (e.g., regular benefit, special authorization) and ensure they complete any necessary requirements within their jurisdiction to prescribe naltrexone or acamprosate. Additional patient criteria may need to be met and regular reporting may be required.

#### 6.2.iv Extended-Release Naltrexone

In the United States, naltrexone is available as an extended-release formulation administered via monthly intramuscular injections,<sup>488</sup> which may promote improved treatment adherence in comparison to daily-dosed oral naltrexone.<sup>517</sup> **Extended-release naltrexone is not currently available in Canada.** Several RCTs have found extended-release naltrexone to be well-tolerated and superior to placebo in terms of improved treatment adherence and retention rates, increased abstinence rates, and decreased alcohol cravings.<sup>517,518</sup> A 2020 meta-analysis (N = 7, n = 1,500) that investigated the effects of extended-release naltrexone compared

to placebo found extended-release naltrexone significantly reduced the number of drinking days (weighted mean difference [WMD] = -2.0, 95% CI: -3.4 to -0.6;  $p = .03$ ) and heavy drinking days per month (WMD = -1.2, 95% CI: -0.2 to -2.1;  $p = .02$ ). Trials that did not require abstinence prior to initiating treatment were associated with greater reductions in monthly heavy drinking days (WMD = -2.0, 95% CI: -3.52 to -0.48;  $p = .01$ ), as were trials that were longer than 3 months (WMD = -1.9; 95% CI: -3.2 to -0.5;  $p = .001$ ).<sup>519</sup> Additionally, given the established body of evidence supporting the use of extended-release naltrexone for the treatment of opioid use disorder (OUD),<sup>520</sup> this medication may have advantages for treatment of individuals with co-occurring AUD and OUD.<sup>521</sup>

## 6.2.v Section Summary and Recommendation

This guideline recommends that all adult patients with moderate or severe alcohol use disorder should be offered evidence-based pharmacotherapy for AUD. Additionally, regardless of AUD severity, the guideline committee recommends that any patient who has stopped or reduced drinking but is continuing to experience strong alcohol cravings or is at risk of return to alcohol use may be an appropriate candidate for pharmacotherapy.

The committee recommends naltrexone and acamprosate as first-line pharmacotherapy options for treatment of AUD. The committee recommends naltrexone for patients with a treatment goal of reduced drinking or abstinence, and acamprosate for patients with a treatment goal of abstinence, based on research evidence supporting each medication's efficacy for achieving these specific outcomes.<sup>261,479,516</sup>

## Recommendation 10

Adult patients with moderate to severe AUD should be offered naltrexone or acamprosate as a first-line pharmacotherapy to support achievement of patient-identified treatment goals.

- A. Naltrexone is recommended for patients who have a treatment goal of either abstinence or a reduction in alcohol consumption.
- B. Acamprosate is recommended for patients who have a treatment goal of abstinence.

HIGH Quality of Evidence

STRONG Recommendation

### Remarks

- Naltrexone may be contraindicated in patients who use or will be using opioids (e.g., opioid agonist treatment, required for surgery). Opioids should be stopped 7–10 days prior to treatment. Other contraindications include a known sensitivity to the drug or its constituents, and patients with acute hepatitis or liver failure. Caution is advised in prescribing naltrexone to patients with liver disease, patients who are pregnant, and patients under the age of 18.
- Acamprosate is contraindicated in patients with severe renal impairment (i.e., creatinine clearance  $\leq$  30 mL/min), patients with a known hypersensitivity to the drug or its constituents, and in patients who are breastfeeding. Caution is advised in prescribing naltrexone to patients with renal disease, patients who are pregnant, patients under the age of 18, and patients over the age of 65.
- Side effects, patient history with naltrexone or acamprosate, and feasibility (e.g., dosing schedules, out-of-pocket costs) should also be considered. For example, acamprosate dosage requires three times daily administration, which may not be preferred by some patients.
- The quality of evidence for this recommendation was rated as high based on multiple systematic reviews that indicated naltrexone is effective for reducing alcohol consumption and maintaining abstinence and acamprosate is effective for maintaining abstinence. The NNT to prevent one person from returning to any drinking was 20 for naltrexone and 12 for acamprosate, while the NNT to prevent return to heavy drinking was 12 for naltrexone and acamprosate did not differ from placebo. Based on this evidence, clinicians should be aware that naltrexone and acamprosate alone will not be effective for all patients.
- The strength of this recommendation was rated as strong based on the quality of evidence, working group consensus, cost-effectiveness, and the effectiveness of naltrexone and acamprosate.

## 6.3 Alternative and Emerging Pharmacotherapies for AUD

Not all individuals with AUD benefit from first-line treatment approaches, despite good adherence and treatment motivation. For example, systematic reviews have reported that 38% to 70% of individuals treated with acamprosate or naltrexone do not benefit or only partially benefit from a trial with one of these medications.<sup>487</sup> As a result, research into alternative pharmacotherapies is ongoing, with the goal of providing a wider range of personalized pharmacotherapy options for individuals seeking treatment for AUD. The research evidence for efficacy and safety of several alternative pharmacotherapies—topiramate, gabapentin, disulfiram, baclofen, and ondansetron—is reviewed below (see [Appendix 5: AUD Pharmacotherapy](#) for summary).

With the exception of disulfiram, which is a Health Canada-approved medication for AUD, use of the medications reviewed below would be considered “off-label.” As with any off-label medication, it is important to conduct a full assessment, including carefully reviewing concomitant medications for potential drug–drug interactions, and documenting patient consent in their chart. Clinicians should discuss prescription coverage with their patient and consult their provincial or territorial formulary to confirm coverage requirements prior to prescribing.




In addition, as comparative safety and efficacy of these alternative therapies has not been fully established in adolescent, pregnant, older adult, or more complex patient populations (e.g., concurrent medical or mental health conditions, co-occurring substance use disorders), prescribing these medications in these cases would be at the clinician’s discretion following a careful assessment of risks, benefits, drug–drug interactions, and contraindications (particularly for pregnant individuals).

### 6.3.i Topiramate

Topiramate is an anticonvulsant medication that has been investigated off-label for treating AUD. A 2021 systematic review found topiramate increased the number of days abstinent compared to placebo or cognitive behavioural therapy (CBT), although evidence supporting topiramate’s effect on cumulative abstinence was reported as being more limited.<sup>522</sup> Across meta-analyses, the topiramate

groups also showed improvements in reduced drinking outcomes (i.e., heavy drinking days, drinks per drinking day, or average number of drinks per day) compared to placebo or treatment as usual (e.g., CBT, naltrexone). A 2020 meta-analysis (N = 64) found that, compared to placebo, topiramate increased the odds of maintaining abstinence up to 12 months (OR = 1.88, 95% CI: 1.06 to 3.34) and reduced treatment dropout (OR = - 0.45, 95% CI: 0.24 to 0.83).<sup>489</sup> A 2014 meta-analysis of 7 placebo-controlled trials (n = 1,125) of topiramate for treating AUD reported significant, moderate-sized effects on aggregate measures of abstinence (Hedges' *g* = 0.438. [medium effect size], *p* < .01) and heavy drinking (Hedges' *g* = 0.406 [medium effect size], *p* < .01), and non-significant effects on gamma-glutamyl transferase (GGT) levels and craving outcomes, compared to placebo.<sup>523</sup> Topiramate doses ranged from 100–300mg/day and duration of treatment from 12–16 weeks. Of note, 3 of the trials included in this review enrolled participants who were not abstinent from alcohol at treatment onset<sup>524-526</sup> and outcomes did not appear to systematically differ from trials that required participants to be abstinent at treatment start.<sup>527-530</sup> In addition, pooled results from 3 randomized trials directly comparing topiramate to naltrexone suggest that topiramate may be superior to naltrexone for heavy drinking and craving outcomes, and equally effective for abstinence-related outcomes.<sup>529,531,532</sup>

## TOPIRAMATE<sup>523</sup>

STUDY		RESULTS	
Intervention	300 mg topiramate for 3 months	 <b>Abstinence</b> <i>medium effect p&lt;.01</i>	
Compared to	Placebo	 <b>Heavy drinking</b> <i>medium effect p&lt;.01</i>	
Study type	Meta-analysis (7 RCTs, n=1,125)	 <b>Craving</b> <i>no effect</i>	



Topiramate is generally well-tolerated, but some individuals do experience significant side effects, particularly at higher doses or with more rapid increases in dosage.<sup>524,525,528,530</sup> For this reason, a gradual dose titration over several weeks is strongly recommended (e.g., approximately 5–8 weeks to full dose).<sup>524,525,528,530</sup> In placebo-controlled trials, adverse effects that were significantly more common with topiramate were paresthesia (50.8% vs. 10.6% in the placebo group), dysgeusia (23.0% vs. 4.8%), anorexia (19.7% vs. 6.9%), difficulty with concentration or attention (14.8% vs. 3.2%), nervousness (14.2% vs. 7.5%), dizziness (11.5% vs. 5.3%), and pruritus (10.4% vs. 1.1%).<sup>525</sup> Clinical experience suggests that rates of side effects such as dizziness, fatigue, and drowsiness may be higher than the rates reported in the product monograph. Most clinical trials conducted to date have used a relatively high daily dose of topiramate (up to 300mg per day); however, one randomized trial that compared psychotherapy alone to psychotherapy plus low-dose topiramate (up to 75mg per day) found that participants who received topiramate were more likely to remain continuously abstinent during a 4-month follow-up period than those who did not (33.3% compared to 14.5%).<sup>533</sup> Further research is needed to determine optimal dosing strategies, rates of dose titration, and maintenance dose levels that best balance treatment effectiveness with patient comfort and safety.

### 6.3.ii Gabapentin

Gabapentin is an anticonvulsant medication that can be used for the management of alcohol withdrawal symptoms and has been studied as an off-label treatment for AUD. A 2019 meta-analysis (7 RCTs, n = 751) concluded that while gabapentin appears to be more efficacious than placebo for treating AUD, the only outcome measure that clearly favors gabapentin is a reduction in the percentage of heavy drinking days (Hedges'  $g = -0.64$  [medium effect size], 95% CI: -1.22 to -0.06).<sup>534</sup> This finding was confirmed in a systematic review published in 2019 (N = 13, n = 807)<sup>535</sup> and a meta-analysis published in 2020 (N = 8, n = 826).<sup>348</sup> The 2020 meta-analysis found gabapentin to be significantly superior to placebo in terms of decreasing the percentage of heavy drinking days (Hedges'  $g = 0.5478$  [medium effect size], 95% CI: 0.0145 to 1.0812;  $p = .044$ ). However, there was no significant difference between treatment with gabapentin and placebo on an aggregated efficacy measure that was calculated using various abstinence or alcohol consumption outcomes.<sup>348</sup> The 2019 systematic review found that gabapentin

reduced alcohol consumption, minimized cravings, and decreased alcohol-related insomnia, with the majority of studies demonstrating efficacy at a relatively high dose of gabapentin (1,200–3,200mg/day).<sup>535</sup> As underscored by these systematic reviews and meta-analyses, further research is needed to definitively establish the safety and efficacy of gabapentin in comparison to first-line and other alternative treatment options.

GABAPENTIN <sup>534</sup>	
STUDY	RESULTS
Intervention	600-3,600 mg gabapentin for 3-26 weeks
Compared to	Placebo
Study type	Meta-analysis (7 RCTs, n=751)

**Abstinence**  
 *no effect*  
 **% Heavy drinking days**  
 *medium effect p=.03*

In a subsequent 2020 RCT (n = 96) that randomized participants to receive gabapentin (1200mg/day) or placebo for 16 weeks, 18.6% more of the gabapentin group reported no heavy drinking days (95% CI: 3.1 to 34.1;  $p = .02$ ; NNT = 5) and 13.8% more reported days with total abstinence (95% CI: 1.0 to 26.7;  $p = .04$ ; NNT = 6) compared to the placebo group.<sup>536</sup> Findings further suggest that, when treated with gabapentin compared to placebo, individuals with high alcohol withdrawal scores had significantly less relapse to heavy drinking (NNT = 3;  $p < .02$ ) and more total abstinence days (NNT = 3;  $p = .003$ ), while those with low alcohol withdrawal scores had similar relapse to heavy drinking (number needed to harm [NNH]<sup>ak</sup> = 25;  $p = .67$ ) and abstinence rates (NNH = 23;  $p = .32$ ), suggesting gabapentin may be more efficacious in patients with a history of alcohol withdrawal symptoms. As gabapentin has also been found to be effective for the outpatient management of

ak Number needed to harm (NNH) corresponds to the number of individuals who must be treated for one individual to experience an adverse outcome.

mild to moderate alcohol withdrawal symptoms,<sup>537</sup> having the option to continue its use beyond the acute withdrawal period as part of a long-term treatment strategy may have advantages (e.g., previous positive response to medication, patient comfort with medication).

In addition to the immediate-release formulation of gabapentin, there is also an extended-release formulation. A 2019 multi-site RCT (n = 346) evaluated the safety and efficacy of an extended-release gabapentin formulation (gabapentin enacarbil) for treating AUD.<sup>538</sup> Participants were randomized to receive either placebo or gabapentin enacarbil (600mg twice per day) for 6 months. At the conclusion of the trial, the percentage of participants with no heavy drinking days did not differ significantly between treatment and placebo (28.3% vs. 21.5%), and no clinical benefit was found for other drinking measures (percent participants abstinent, percent days abstinent, percent heavy drinking days, drinks per week, drinks per drinking day), alcohol craving, alcohol related consequences, sleep problems, smoking, and depression/anxiety symptoms.<sup>538</sup> The lack of a demonstrated treatment effect for the extended-release formulation compared to earlier trials of immediate-release gabapentin is not yet fully understood, and more research is needed—in particular, large, well-designed, multi-site trials that directly compare different gabapentin formulations and dosages.<sup>538</sup> At this time, based on these results, extended-release gabapentin<sup>al</sup> is not recommended for the treatment of AUD.

The most common adverse events reported in placebo-controlled clinical trials of (immediate-release) gabapentin are dizziness (19.1% vs. 6.6% in the placebo group), somnolence (14.1% vs. 5.2%), ataxia or gait disorder (14.0% vs. 2.2%), and peripheral edema (6.6% vs. 1.5%).<sup>539</sup> As gabapentin is excreted renally, it is safe to use in patients with severe liver disease, but conservative dosing is required in patients with severe renal failure. In patients with chronic kidney disease, glomerular filtration rate (GFR) should be monitored with gabapentin dosage adjusted as needed with any changes in GFR.<sup>540</sup> Due to its side effect profile, caution is advised in prescribing gabapentin to patients at increased risk of confusion, disorientation or falls (e.g., older adults, frail patients, individuals with cognitive impairment).

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al Extended-release gabapentin is not currently available in Canada.

### 6.3.ii.1 Safety Considerations for Gabapentin

Recent reports have raised concerns regarding potential risks of non-medical use, physiological dependence, and withdrawal syndromes associated with gabapentin.<sup>541-546</sup> While large observational cohort studies in the United Kingdom and the United States have shown that the prevalence of non-medical use of gabapentin is low in the general population (1%)<sup>547</sup> and among individuals prescribed gabapentin (2%),<sup>548</sup> higher rates (12–22%) have been documented among opioid-using populations and in facilities where access to alcohol and other drugs is restricted (e.g., inpatient treatment programs, correctional facilities).<sup>546,548-551</sup> A 2016 review identified 18 case reports and case series describing non-medical use including non-prescribed (diverted) use and use where not taken as prescribed (e.g., higher or more frequent doses; combined with other substances; or taken by inhalation, injection, or other routes), as well as physiological dependence or withdrawal symptoms on discontinuation of use.<sup>552</sup> Gabapentin dependence was noted only among patients with a history of alcohol, stimulant, or opioid use disorders, and the average daily dose in these cases was approximately 3000mg/day (range 600–8000mg/day).<sup>552</sup> Withdrawal symptoms, where reported, occurred within 12 hours to 7 days of discontinuation of gabapentin, and included restlessness, disorientation, confusion, agitation, and anxiety, which did not resolve with the administration of benzodiazepines.<sup>552</sup>

There have also been a small number of reports of individuals combining high doses of gabapentin with alcohol or other medications (such as quetiapine, buprenorphine/naloxone, methadone, and other prescribed or unregulated opioids) to potentiate euphoric effects.<sup>553-557</sup> The combined use of opioids and gabapentin is of particular concern, due to additive effects on respiratory depression, which can increase risk of fatal overdose.<sup>558</sup> A 2017 Canadian study of 5,875 individuals prescribed opioid medications reported that concomitant use of prescribed gabapentin increased the risk of fatal overdose by 49% (adjusted odds ratio [aOR] = 1.49, 95% CI: 1.18 to 1.88;  $p < .001$ ) compared to case-controls (matched for age, sex, index year, history of chronic kidney disease, and disease risk index).<sup>559</sup> The study also found evidence that moderate (900–1800mg) and high ( $\geq 1800$ mg) prescribed daily doses of gabapentin increased the adjusted odds of a fatal opioid overdose by 60% (aOR = 1.56, 95% CI: 1.06 to 2.28;  $p = .024$  for moderate doses; aOR = 1.58, 95% CI: 1.09 to 2.27;  $p = .015$  for high doses) compared to individuals with no concomitant gabapentin use.<sup>559</sup> Gabapentin is also increasingly being

identified in post-mortem toxicology analyses of individuals who have died from substance-related overdoses.<sup>546</sup> For example, a 2018 analysis of 4,169 overdose deaths in 5 US states reported that gabapentin was detected in 22% of all overdose deaths and 26% of opioid-related overdose deaths.<sup>560</sup>

It is likely that the risks of non-medical gabapentin use in individuals with AUD remain lower than risks associated with untreated AUD for those patients for whom first-line pharmacotherapies and other second-line pharmacotherapies are not appropriate or preferred. However, primary care providers do need to be aware of these risks and carefully monitor their patients for any signs of non-medical use, dependence, and diversion, with particular attention to individuals prescribed multiple medications for concurrent medical conditions. If diversion or not taking as prescribed is a concern, clinicians can consider prescribing gabapentin to be dispensed daily, weekly or biweekly from a pharmacy, or with blister-packaging to conduct random pill counts.<sup>542</sup>

### 6.3.iii Disulfiram

As noted above, disulfiram is one of three Health Canada-approved medications for treatment of AUD in adults; however, disulfiram is not commercially available in Canada and must be compounded by specialty pharmacies. Unlike other AUD pharmacotherapies, disulfiram does not directly influence the neural pathways linked to the rewarding effects of, cravings for, or motivation to drink alcohol. It is an aversive agent that causes an extremely unpleasant physiological reaction if alcohol is consumed (i.e., an alcohol-disulfiram reaction). Disulfiram blocks the metabolism of alcohol by inhibiting the aldehyde dehydrogenase enzyme, which results in an accumulation of acetaldehyde (the primary metabolite of alcohol) in the body.<sup>488</sup> Acetaldehyde causes a range of side effects that may include sweating, headache, dyspnea, lowered blood pressure, flushing, sympathetic hyperactivity, heart palpitations, nausea, and vomiting.<sup>488</sup> This reaction can occur if alcohol is consumed for up to 2 weeks after a standard daily dose (125–500mg) of disulfiram is taken.<sup>488</sup> As the alcohol-disulfiram reaction can potentially be fatal, patients must never be administered disulfiram without full consent and knowledge of its effects.<sup>561</sup>

Placebo-controlled trials have not clearly demonstrated that disulfiram is more effective than placebo for the treatment of AUD. A 2014 meta-analysis of 2 clinical trials ( $n = 492$ ) did not find any significant differences between disulfiram and placebo in preventing a return to any drinking among individuals with AUD.<sup>261</sup> Previous studies have noted that disulfiram adherence rates are low, which contributes to its lack of efficacy.<sup>562</sup> In contrast, a 2014 meta-analysis ( $N = 22$  RCTs,  $n = 2,414$ ) that examined the impact of supervision of medication compliance found that disulfiram had significant benefits on abstinence (defined in various ways in each study) in only in supervised conditions (Hedges'  $g = 0.82$  [large effect size], 95% CI: 0.59 to 1.05;  $p < .001$ ).<sup>563</sup> A 2007 open label clinical trial ( $n = 243$ ) that randomly assigned participants to receive 12 weeks of disulfiram, naltrexone, or acamprosate treatment under supervision found that individuals taking disulfiram had greater time to first heavy drinking days ( $p = .0002$ ), and greater reductions in average weekly consumption ( $p < .0001$ ) and number of days abstinent ( $p < .0001$ ) compared to either naltrexone and acamprosate.<sup>564</sup> However, the relative benefits of disulfiram observed during the trial dissipated in a subsequent unsupervised 52-week treatment period, a setting that may more closely resemble “real-world” conditions.<sup>564</sup>

Based on this evidence, disulfiram is not recommended over other available pharmacotherapies for AUD that have been proven effective in preventing relapse or reducing alcohol consumption. However, it is recognized that some individuals may be interested in this approach for a variety of reasons. For example, some individuals may wish to take disulfiram as an additional source of support in avoiding alcohol consumption in certain circumstances (e.g., vacations, special occasions, other occasions where individuals might consume alcohol in ways that do not align with their treatment goal) or occupations (e.g., safety-sensitive positions). In these cases, the evidence of risks and benefits must be carefully reviewed, and education on adverse effects that may be experienced if alcohol is consumed (including accidental/incidental exposure to non-beverage alcohol) must be provided to patients and families prior to initiating treatment. “Disulfiram contracts,” in which a patient and their partner agree to practice daily witnessed disulfiram ingestion with verbal reinforcement by the partner, in conjunction with couples therapy, have been shown to increase compliance with the medication and improve abstinence rates.<sup>565</sup> As clinical trials indicate that disulfiram is most effective when taken under structured and supervised conditions, disulfiram

should only be prescribed to patients who are engaged in ongoing addiction care where safety monitoring pathways are in place and adherence can be assessed regularly by a health care provider or other reliable individual.

Side effects of disulfiram (in the absence of alcohol) are typically mild, and include fatigue, mild drowsiness, headache, and dermatitis.<sup>488</sup> Although infrequent, hepatotoxicity has been reported in patients with and without prior history of abnormal liver function; baseline and follow-up liver function tests (LFT) should be routinely requested during treatment, and patients and families should be advised to immediately report early signs or symptoms of hepatitis.<sup>561</sup> Contraindications to disulfiram use include severe myocardial disease or coronary occlusion, psychosis, or known hypersensitivity to the medication.<sup>488</sup> Patients must never be administered disulfiram without full consent and knowledge of its effects.<sup>561</sup> As the disulfiram–alcohol reaction can present as an emergency, use of disulfiram to reduce drinking rather than sustain abstinence is not appropriate or recommended.

### 6.3.iv Baclofen

Baclofen is a GABA receptor agonist that is primarily prescribed as a muscle relaxant, but has also been used to treat AUD. While not commonly prescribed in North America, it is an approved AUD pharmacotherapy in France and commonly used off-label in Australia and Germany.<sup>566</sup> As baclofen is not metabolized in the liver, it was initially studied as a treatment option for individuals with severe AUD diagnosed with acute hepatitis, liver disease, and cirrhosis.<sup>567</sup> Although early trials in this population showed some promise,<sup>568,569</sup> subsequent studies have yielded mixed results.<sup>570-574</sup>

A 2023 Cochrane review (N = 17, n = 1,818) found that baclofen is likely to reduce the risk of relapse and increase the percentage of days abstinent, predominantly in patients that have undergone detoxification.<sup>575</sup> There was no difference between baclofen and placebo for other primary outcomes (e.g., heavy drinking days, drinks per drinking day) and secondary outcomes (e.g., alcohol craving, anxiety, depression). There was limited data and uncertain evidence for any differences between baclofen and naltrexone or acamprosate. Earlier meta-analyses published in 2018 and 2021 reported similar outcomes, though results

were not stratified by completed withdrawal versus active drinking status. A meta-analysis from Pierce et. al. (N = 13, n = 1,492) reported that baclofen was superior to placebo for some outcomes (time to return to drinking, percentage days abstinent), but not for overall abstinence rates.<sup>576</sup> A meta-analysis from Rose et. al. (N = 12, n = 590) reported that baclofen was associated with higher rates of abstinence than placebo but no difference in other outcomes (days abstinent, heavy drinking, craving).<sup>577</sup> A 2020 meta-analysis (N = 13, n = 983) found that baclofen was more effective in increasing days abstinent among patients with higher baseline anxiety levels.<sup>578</sup> In contrast, one 2018 meta-analysis (N = 14, n = 1,522) found no difference between baclofen and placebo in abstinence rates or alcohol consumption.<sup>579</sup>

Compared to placebo, baclofen is associated with increased rates of side effects including vertigo, drowsiness, paraesthesia (“pins and needles” sensation), and muscle spasms or rigidity.<sup>580</sup> Safety concerns have also been raised with off-label use of baclofen.<sup>581</sup> For example, a 2018 French national registry study (n = 165,334) found that baclofen was associated with a dose-dependent increased risk of hospitalization (HR = 1.13, 95% CI: 1.09 to 1.17) and death (HR = 1.31, 95% CI: 1.08 to 1.60) compared to other AUD pharmacotherapies approved in France (naltrexone, nalmefene, acamprosate).<sup>582</sup> Overall, there is lack of clear evidence regarding the effectiveness of baclofen for the treatment of AUD, particularly as an ongoing treatment or in comparison to first-line pharmacotherapies. However, baclofen could be considered for patients who have undergone withdrawal and for whom other medications are contraindicated.

### 6.3.v Ondansetron

Ondansetron is a selective serotonin receptor (5-HT<sub>3</sub>) antagonist approved for the treatment of nausea associated with chemotherapy and has also been studied for treating AUD. Based on the findings of several small pilot trials and human laboratory studies,<sup>583</sup> ondansetron appears to be selectively effective in 2 specific subsets of patients: individuals who developed an AUD at ≤ 25 years of age,<sup>584</sup> and individuals who have a genetic variant of the serotonin transporter gene (5-HTT).<sup>585</sup> These findings have yet to be replicated in a large, multi-site clinical trial.<sup>586</sup> An initial 1994 clinical trial (n = 71) that did not differentiate participants



based on age of onset of AUD or by genotype found no significant difference in alcohol consumption between individuals who received a 6-week trial of ondansetron versus those who received placebo.<sup>587</sup>

Side effects most frequently reported in clinical trials of ondansetron for AUD include diarrhea, headache, and fever. Ondansetron prolongs the QT interval in a dose-dependent manner and should not be prescribed to patients with underlying cardiac conditions, such as congenital long QT syndrome, cardiac hypertrophy, or those taking other medications associated with QT prolongation.<sup>588,589</sup>

### **6.3.vi Combination Pharmacotherapy**

Combination pharmacotherapy is often used in various disorders that do not respond to monotherapy, and there is growing interest in applying similar approaches to AUD. Theoretically, combining AUD pharmacotherapies could address a broader range of symptoms or augment the modest treatment effects that have been observed with AUD monotherapies in research studies and clinical practice.

A 2018 meta-analysis of 16 RCTs evaluating combination pharmacotherapy for the treatment of AUD concluded that no significant benefits were observed for the use of combinations over single medications alone in terms of alcohol-related outcomes, but noted that the current evidence base is limited.<sup>590</sup> Few well-controlled studies have been conducted in this area, and studies that have been published are limited by small sample sizes, low power, imprecise measures of treatment effects, and other methodological flaws.<sup>590</sup> More research is needed to determine the value of combination therapy. Select research evidence on safety and efficacy of two promising examples of combination AUD pharmacotherapy is reviewed below.

#### **6.3.vi.1 Naltrexone and Acamprosate**

A 2003 RCT that randomized 160 participants to 4 treatment conditions for 12 weeks reported relapse rates of 75% for placebo, 50% for acamprosate, 35% for naltrexone, and 28% for combined acamprosate-naltrexone therapy.<sup>510</sup> Significance tests showed that combination therapy was superior to acamprosate, but not naltrexone monotherapy, for the prevention of relapse to any drinking ( $p = .04$ ) and

heavy drinking ( $p = .04$ ).<sup>510</sup> In a 2020 meta-analysis ( $N = 60$ ), combined naltrexone-acamprosate therapy demonstrated greater effectiveness in maintaining abstinence for up to 12 months ( $OR = 3.68$ , 95% CI: 1.50 to 9.02) and reducing treatment dropout ( $OR = 0.30$ , 95% CI: 0.13 to 0.67) compared to placebo.<sup>489</sup> In contrast, results from the 2006 Combined Pharmacotherapies and Behavioural Interventions for Alcohol Dependence (COMBINE) trial, in which 1,383 patients were randomized to 9 treatment groups, did not show combination therapy to be more effective than naltrexone or acamprosate alone, cognitive behavioural therapy, or placebo among participants also receiving medical management (e.g., counselling to promote medication adherence, prevent relapse, and support recovery).<sup>402</sup> In both trials, combination therapy was well-tolerated, with only minor adverse effects (e.g., nausea) observed to occur more frequently in comparison to either medication alone.<sup>402,510</sup> Given the limited research, there is insufficient evidence to recommend combined naltrexone and acamprosate therapy.

### 6.3.vi.2 Naltrexone and Gabapentin

One RCT has evaluated whether the combination of naltrexone (50mg per day) and gabapentin (up to 1200mg per day) resulted in greater abstinence rates and lower alcohol consumption during the early stages of alcohol cessation than naltrexone alone or placebo.<sup>591</sup> In this 2011 trial, 150 individuals were randomly assigned to receive a 16-week course of naltrexone alone, naltrexone with gabapentin added for the first 6 weeks, or double placebo.<sup>591</sup> During the first 6 weeks, the naltrexone-gabapentin group had a longer interval to heavy drinking than the naltrexone monotherapy group ( $p = .04$ ), which was comparable to the placebo group.<sup>591</sup> The naltrexone-gabapentin group also had fewer heavy drinking days than the naltrexone monotherapy group ( $p < .001$ ) and fewer drinks per drinking day than the naltrexone monotherapy ( $p = .02$ ) and placebo groups ( $p = .01$ ).<sup>591</sup> After gabapentin was discontinued, there were no differences between treatment and placebo groups in alcohol-related outcomes.<sup>591</sup> A history of alcohol withdrawal was associated with better treatment outcomes in the naltrexone-gabapentin group.<sup>591</sup> The combination was well-tolerated with the most commonly reported side effects being dizziness and daytime sedation.<sup>591</sup> While these results are promising, there is a need for larger, multi-site trials to confirm that the combination of naltrexone and gabapentin is safe and efficacious for the treatment of AUD, and to clarify optimal dosing and duration of combination therapy.

### 6.3.vii Pharmacogenetic Approaches to AUD Pharmacotherapy

Recent advances in the field of genetics have led to the identification of several candidate genetic polymorphisms that may predict individual responses to medications for treating AUD.<sup>592</sup> In some cases, initial studies have shown promise, but larger, more robust prospective studies have failed to demonstrate an association between genetic markers and treatment response. For example, several *post-hoc* analyses of cohort studies found that individuals with a specific polymorphism in the Asn40Asp gene responded more favourably to naltrexone,<sup>593-596</sup> but a subsequent large and well-powered trial found no evidence of any gene-treatment interaction effects.<sup>597</sup> Although use of pharmacogenetics is not feasible for treatment-matching at the present time, several pharmacogenetic studies are currently underway<sup>598-602</sup> and hold potential for more targeted “personalized medicine” approaches to AUD treatment in the future.

### 6.3.viii Section Summary and Recommendation

This guideline recommends that pharmacotherapy with topiramate and gabapentin be considered on a case-by-case basis for patients who do not benefit from treatment with first-line therapy with naltrexone or acamprosate, have contraindications to their use, or express a preference for an alternative medication. Although the evidence bases for topiramate and gabapentin are more limited than that of first-line therapies, research suggests that these medications are safe and effective in reducing alcohol consumption in some patients.

For topiramate, this recommendation is based on moderate quality evidence from several meta-analyses and clinical trials that have demonstrated that topiramate is associated with clinically significant improvements in multiple alcohol-related outcomes, with some evidence that treatment effect sizes are comparable or greater than those observed with naltrexone.<sup>261,523</sup> For gabapentin, the recommendation is based on a limited but promising body of evidence for efficacy,<sup>537</sup> and it has demonstrated advantages in the treatment of symptoms associated with protracted alcohol withdrawal (e.g., insomnia, anxiety).<sup>603</sup> The committee notes that clinicians should be aware of the potential for non-medical use and diversion of gabapentin and employ risk mitigation strategies if necessary (e.g., blister-packs, short-course prescriptions, witnessed ingestion at pharmacy).

This recommendation is also aligned with other published guidelines. For example, topiramate has been recommended as a first-line treatment (along with disulfiram, acamprosate, and naltrexone) for AUD in the US Department of Veterans Affairs/ Department of Defense (VA/DoD) *Clinical Practice Guideline for the Management of Substance Use Disorders*.<sup>189</sup> Additionally, the American Psychiatric Association's *Practice Guideline for the Pharmacological Treatment of Patients With Alcohol Use Disorder* recommends topiramate or gabapentin for treatment of patients with AUD who would prefer these medications or who have not benefited from first-line medications (naltrexone or acamprosate).<sup>604</sup>

The committee does not recommend disulfiram over other available pharmacotherapies for AUD due to comparatively weak evidence of efficacy. However, it is recognized that some individuals may express a preference for this medication, for example, individuals seeking additional support to avoid alcohol in certain circumstances (e.g., special occasions) or occupations (e.g., safety-sensitive positions). As clinical trials indicate that disulfiram is most effective when taken under structured and supervised conditions, disulfiram can be offered to patients who are engaged in ongoing addiction care where adherence can be monitored by a health care provider or other reliable individual.

At this time, there is insufficient evidence to recommend use of ondansetron. Alternatively, for those wishing to pursue abstinence and who have undergone detoxification, some evidence suggests baclofen could be considered. Further research is also needed before evidence-based recommendations can be made regarding combination pharmacotherapy. Clinicians are encouraged to consult with an addiction medicine specialist for expert guidance and decision support if considering one of these treatment approaches.

## Recommendation 11

Adult patients with moderate to severe AUD who do not benefit from, have contraindications to, or express a preference for an alternate to first-line medications can be offered topiramate or gabapentin.

**MODERATE** Quality of Evidence (**topiramate**)  
**LOW** Quality of Evidence (**gabapentin**)

**STRONG** Recommendation (**topiramate**)  
**CONDITIONAL** Recommendation (**gabapentin**)

### Remarks

- Selection of an appropriate medication should be made through a shared decision-making process between patient and provider after reviewing evidence of benefits and risks, and in the context of the patient's goals, needs, and preferences.
- Topiramate is contraindicated in patients with a known hypersensitivity to the drug or its constituents and in patients who are pregnant or planning to become pregnant. Caution is advised in prescribing topiramate to patients a) with renal disease or failure, b) with hepatic disease, c) under the age of 18, and d) over the age of 65. Due to dose-dependent risk of significant CNS side effects, dose should be gradually titrated upwards over a period of 4–8 weeks.
- Gabapentin is contraindicated in patients with a known hypersensitivity to the drug or its constituents. Caution is advised in prescribing gabapentin to patients a) with cognitive impairment, b) taking opioids (prescribed or non-medical use), c) who are pregnant or breastfeeding, d) under the age of 18, and e) over the age of 65.
- Side effects, feasibility (e.g., dosing schedules, out-of-pocket costs), and patient history with topiramate or gabapentin should also be considered.
- As with any medication prescribed off-label, it is important to conduct a full assessment, including careful review of concomitant medications for potential drug–drug interactions, and to clearly document patient consent prior to initiating treatment.
- The quality of evidence for the recommendation on topiramate was rated as moderate based on several systematic reviews, meta-analyses, and clinical trials that have demonstrated topiramate is associated with clinically significant improvements in multiple alcohol-related outcomes, with some evidence that effect sizes are comparable or greater to those observed with naltrexone.
- The strength of the recommendation for topiramate was rated as strong based on the quality of evidence, working group consensus, cost-effectiveness, and the effectiveness of topiramate.
- The quality of evidence for the recommendation on gabapentin was rated as low based on a limited but promising evidence base supporting its efficacy and demonstrated benefits for decreasing heavy drinking days.
- The strength of the recommendation for gabapentin was rated as conditional based on the quality of evidence, working group consensus, cost-effectiveness, and the effectiveness of gabapentin, as well as the potential for dependence and non-medical use. Clinicians should consider the potential risks and benefits associated with gabapentin when developing a treatment plan.

## 6.4 Duration of Treatment

There is a lack of research evidence to guide the optimal duration of AUD pharmacotherapy. Because AUD can be a chronic, relapsing condition, and as emphasized in this guideline, an ongoing and individually tailored approach to

**AUD pharmacotherapy should be prescribed for at least 6 months. Medications can be continued if patient and provider decide there is benefit.**

clinical management is required. Most clinical practice guidelines recommend that AUD pharmacotherapy be prescribed for at least 6 months, at which point the utility of continuing treatment can be reassessed in collaboration with the patient.<sup>189,488,604</sup> If deemed clinically necessary, medications can be continued indefinitely unless safety concerns arise.<sup>605</sup>

## 6.5 Pharmacotherapy Options for Youth

Although medications are often used off-label to treat a range of psychiatric conditions in youth, they are infrequently prescribed for substance use disorders, and treatment of youth has traditionally consisted of psychosocial treatment alone.<sup>606</sup> While several psychosocial treatment interventions have been shown to be effective in youth with AUD (see [Psychosocial Treatment Interventions in Youth](#)), not all individuals benefit from this approach. Reported rates of relapse following psychosocial treatment alone for substance use in youth are high, ranging from 46% to 79% at 12 months post-intervention.<sup>606</sup>

Prospective studies have shown that unrecognized or untreated alcohol use disorder in youth often progresses to more severe forms of AUD and alcohol-related harms in adulthood.<sup>607</sup> Additionally, due to ongoing neurological and cognitive development, there is increasing evidence that adolescents and young adults are particularly susceptible to adverse effects of heavy alcohol consumption on social and behavioural functioning.<sup>246</sup> For these reasons, use of the most effective treatments, including pharmacotherapy, should be considered on a case-by-case basis for treatment of youth with moderate to severe AUD, particularly among those who have not benefited from non-pharmacologic treatment.

Two pilot studies of naltrexone have been conducted among youth. A small 2005 study enrolled 5 youth (mean age =  $16.8 \pm 3.11$  years) diagnosed with moderate to severe AUD in a 6-week open label trial, and reported a significant reduction in alcohol consumption (-7.5 drinks/day) during treatment.<sup>608</sup> A crossover 2014 RCT enrolled 28 youth (aged 15–19) to receive naltrexone and placebo for 8–10 days each, with a washout period in between treatments.<sup>609</sup> The authors found that naltrexone reduced craving under both laboratory and natural conditions (natural:  $p = .02$ ; laboratory:  $p = .04$ ), and it reduced the frequency of any drinking (OR = 0.69, 95% CI: 0.50 to 0.97;  $p = .03$ ) and frequency of heavy drinking (OR = 0.54, 95% CI: 0.35 to 0.81;  $p = .003$ ) under natural conditions.<sup>609</sup> In addition, in 2 open-label randomized trials, one published in 2008 and one in 2014, comparing naltrexone to disulfiram ( $n = 110$ ), youth participants (aged 15–18) who received naltrexone reported significantly lower levels of craving compared to those who received disulfiram.<sup>610,611</sup> In all 4 studies, naltrexone was well-tolerated with few side effects, and no serious adverse events were reported. Acamprosate has not been studied in youth patient populations.

In the absence of a substantive evidence base, clinical practice guidelines recommend that pharmacotherapies approved for treatment of AUD in adults (naltrexone, acamprosate) can be considered on a case-by-case basis for treatment of moderate to severe alcohol use disorder in youth (aged 12–18).<sup>306,488,567,612,613</sup> Alcohol is the most commonly used substance in youth and warrants routine screening, brief intervention, and advice on safer use (see [Screening, Diagnosis, and Brief Intervention](#)).

## 6.6 Pharmacotherapy Options for Pregnant Patients

Due to the lack of evidence of safety and efficacy in pregnancy, it is strongly emphasized that prescribing AUD pharmacotherapy to such individuals should be done in close consultation with a perinatal addiction medicine specialist. Informed consent and shared decision-making with the patient are essential in this context as the balance of risks and benefits will be unique to each individual.

There have been no RCTs or meta-analyses on the safety and efficacy of AUD pharmacotherapies in pregnant individuals. A 2018 case report and literature

review suggests prescribing gabapentin, naltrexone, or acamprostate to pregnant individuals be considered on a case-by-case basis, based on evidence that these medications appear to be compatible with pregnancy (i.e., FDA Category C<sup>am</sup>) and the known maternal/parental and fetal risks of continued alcohol use or relapse in pregnancy.<sup>614</sup> The authors emphasize that the potential risks of medications must be carefully weighed against the known teratogenic risks of alcohol when making treatment decisions.<sup>614</sup> If naltrexone is used, it may reduce the efficacy of opioids used for labour, delivery, and post-partum pain management,<sup>615,616</sup> thus referral to or consultation with an anesthesiologist prior to birth is advised. Following pregnancy, medications for AUD are likely to be transferred into breast milk. There is limited information on the safety of using these medications during breastfeeding, though no adverse effects from naltrexone<sup>617</sup> or gabapentin<sup>372</sup> have been found. If medications are used during breastfeeding, clinicians are advised to monitor the infants regularly. Additional details are available in the [BCCSU AUD Pregnancy Supplement](#).

With regards to other AUD pharmacotherapies reviewed in this guideline, topiramate is contraindicated in pregnancy due to its association with cleft palate if used in the first trimester,<sup>618</sup> and use of disulfiram in pregnancy is strongly recommended against due to the potential risks of a severe disulfiram–alcohol reaction to the fetus.<sup>369</sup> As there is insufficient evidence to support use of baclofen and ondansetron in non-pregnant patients, neither medication would be considered appropriate for use in pregnancy.

## 6.7 Pharmacotherapy Options for Older Adults

Few studies have evaluated AUD pharmacotherapies in older adults (aged 65 and older).<sup>457</sup> An RCT from 1997 (n = 44) found naltrexone was effective at reducing relapse rates among those older adults who drank alcohol during the study ( $p = .024$ ), but did not differ from placebo in terms of abstinence rates or reduced cravings.<sup>619</sup> To date, studies on acamprostate and older adults are not available.<sup>457</sup>

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am FDA Category C: No adequate human studies; Evidence of risk in some animal studies; Potential benefits may still outweigh the risks.



Clinicians should be aware that acamprosate is eliminated from the body through the kidneys. Since older adults have a greater risk of reduced kidney function, clinicians should administer baseline and regular renal function tests for patients prescribed acamprosate.<sup>457</sup> Clinicians should exercise caution and may need to reduce dosage if prescribing disulfiram to older adults as disulfiram interacts with multiple medications.<sup>620</sup> Additionally, older adults who have cognitive impairment or do not have a support person to assist with medications may be less likely to take the medication as prescribed.

In 2019, the Canadian Coalition for Seniors' Mental Health published<sup>140</sup> [Canadian Guidelines on Alcohol Use Disorder Among Older Adults](#). Their recommendations include prescribing naltrexone and acamprosate, as indicated, with attention given to contraindications and side effects. Medications should be started at a low dose and titrated slowly. Pharmacotherapy with appropriate follow-up can be initiated for older adults in any clinical setting, including the community, hospital, long-term care, or following a supervised medical withdrawal program. Gabapentin and topiramate were not recommended for older adults due to limited evidence. Gabapentin is particularly discouraged for older adults, due to the risk of cognitive impairment, sedation, drug interactions, and non-medical use.

## 6.8 Combining Pharmacotherapy and Psychosocial Treatment Interventions

Although the majority of AUD pharmacotherapy trials have also included either medical management, structured psychosocial treatment interventions, or peer support groups as a standard treatment condition, very few studies have been explicitly designed to evaluate whether the combination of pharmacotherapy and psychosocial treatment is more effective than either treatment alone. Similarly, very few trials have assessed whether stepped care strategies, such as varying the intensity of psychosocial treatment or self-defined wellness and recovery-oriented support, can improve pharmacotherapy treatment outcomes, or vice versa.

The 2006 COMBINE trial (n = 1,383) randomized participants to receive 4 months of treatment with either (1) naltrexone, (2) acamprosate, (3) both naltrexone and acamprosate, or (4) placebo.<sup>402</sup> Treatment groups were randomized to receive either medical management or a combined psychosocial treatment intervention

(including elements of motivational interviewing, CBT, and 12-step) delivered by a specialist.<sup>402</sup> At the end of the treatment period, there were no differences in alcohol-related outcomes (percent days abstinent, return to heavy drinking) between the combination of naltrexone and psychosocial treatment compared to groups who received naltrexone or psychosocial treatment alone. There were also no differences in outcomes between acamprosate combined with either naltrexone or psychosocial treatment, and acamprosate combined with both naltrexone and psychosocial treatment when compared to placebo.<sup>402</sup> In contrast, a 2005 single-site trial (n = 160) by the same study team compared naltrexone or placebo combined with motivational enhancement therapy (MET) or CBT in a 4-block RCT design, and showed that participants who received naltrexone and CBT had lower relapse rates, a longer duration of time before returning to drinking, and a longer duration of time between drinking days compared to those treated with naltrexone and MET or psychosocial treatment alone.<sup>621</sup>

**Combining pharmacotherapy and psychosocial therapy may lead to better outcomes than a single intervention.**

A 2018 network meta-analysis (N = 137, n = 27,282) examined the effect of 8 variations of psychotherapy (including CBT, motivational enhancement therapy, or 12-step facilitation), pharmacotherapy, contingency management, brief intervention,

or combinations of these on abstinence rates.<sup>622</sup> Contingency management combined with psychotherapy significantly increased abstinence rates compared with other treatment interventions during treatment (OR = 2.19, 95% CI: 1.29 to 3.72), while pharmacotherapy combined with psychotherapy significantly increased abstinence rates compared with other interventions following treatment (OR = 1.41, 95% CI: 1.08 to 1.84). Psychotherapy alone was not found to be associated with increased abstinence rates during treatment or follow-up compared to controls. Pharmacotherapy alone was the only intervention to significantly increase abstinence rates in both treatment and follow-up sessions. Taken together, the authors suggest these findings support pharmacotherapy and contingency management as key factors in achieving abstinence, although further research to validate this conclusion is required. A 2020 meta-analysis (N = 30 RCTs, n = 3,551; N = 14, n = 2,229 specific to AUD) examined CBT combined with pharmacotherapy and found a benefit compared to usual care and pharmacotherapy. There was a small reduction in substance use frequency (Hedge's  $g = 0.18$  [small effect], 95% CI: 0.01 to 0.35;  $p = .04$ ) and a moderate

reduction in quantity (Hedge's  $g = 0.28$  [medium effect], 95% CI: 0.03 to 0.54;  $p = .03$ ). However, CBT performed similarly to other therapy approaches, and the authors concluded that treatment should include pharmacotherapy plus an evidence-based psychosocial intervention.<sup>623</sup> Overall, results are not consistent; however, there are promising data suggesting that pharmacotherapy combined with a psychosocial intervention can lead to greater improvements alcohol-related outcomes compared to either intervention alone.

Whereas there is limited empirical evidence to guide recommendations on the optimal combination of pharmacotherapy, psychosocial treatment, and self-defined wellness and recovery-oriented services, this guideline supports using an integrated care approach, in which treatment type and intensity are continually adjusted to match the individual patient's needs and circumstances over time. Such a strategy recognizes that many individuals may benefit from the ability to access different psychosocial treatment and wellness and recovery support options at different times. The stepped approach may include treatment intensification (e.g., adding specialized psychosocial treatment to a pharmacotherapy-based strategy, consideration of structured treatment programs), transitions between different treatment options, and strategies to de-intensify pharmacological or psychosocial treatment at the patient's discretion, where the patient can opt to re-initiate pharmacotherapy or psychosocial treatment at any time if needs and circumstances change.

## 6.9 Drug-Drug Interactions

Clinicians should review drug-drug interactions for AUD medications prior to prescribing any medication to a patient. For a comprehensive list of drug interactions, consult each medication's product monograph. UpToDate's [Lexicomp Drug Interactions](#) tool provides information on drug interactions in an electronic platform.

### 6.9.i Naltrexone

Naltrexone should not be prescribed to patients who are taking opioids, either prescribed or illicit. This includes opioids prescribed for opioid agonist treatment for opioid use disorder (e.g., buprenorphine/naloxone, methadone, slow-release

oral morphine). Prescribing naltrexone to an individual taking opioids increases the risk of precipitated withdrawal or potentially fatal overdose if opioids are consumed in an attempt to overcome naltrexone's opiate blockade. The safety and efficacy of combination naltrexone and disulfiram is unknown. The combined use of two potentially hepatotoxic medications is not recommended unless the benefits outweigh the risks.<sup>492</sup>

### **6.9.ii      Acamprosate**

There are few clinically significant drug–drug interactions with acamprosate. When taken in combination with naltrexone, blood levels of acamprosate calcium can be increased; however, no dose adjustment is required. No interaction has been observed in acamprosate administration in combination with alcohol, disulfiram, diazepam, nordiazepam, imipramine, or desipramine. In clinical trials, acamprosate has been administered safely in combination with antidepressants, anxiolytics, hypnotics and sedatives, and non-opioid analgesics.<sup>624</sup>

### **6.9.iii     Topiramate**

Numerous drug–drug interactions have been documented with topiramate. Plasma levels of topiramate or other medications may be significantly affected when administered concomitantly, including some anti-epileptic medications, digoxin, oral contraceptives, hydrochlorothiazide, metformin, glyburide, pioglitazone, lithium, risperidone, amitriptyline, and diltiazem. Concomitant use of topiramate and medications that are predisposing to nephrolithiasis should be avoided due to the increased risk of nephrolithiasis. Interactions between topiramate and CNS depressants have not been studied. The use of topiramate and CNS depressants together is not recommended.<sup>625</sup>

### **6.9.iv      Gabapentin**

Gabapentin has a low level of binding to plasma proteins and is eliminated solely by renal excretion. As a result, there have been few drug interactions observed in

which the pharmacokinetics of gabapentin or other co-administered medications are affected. Effects on the bioavailability of gabapentin and certain medications (i.e., morphine, naproxen, antacids, and cimetidine) have been documented. Gabapentin is additive in the impairment of cognitive and gross motor function caused by opioids, benzodiazepines, and alcohol; respiratory failure, coma, and death have been reported in patients taking gabapentin alone or in combination with other CNS depressants. Patients prescribed gabapentin in combination with opioids should be monitored for signs and symptoms of respiratory depression and sedation.<sup>626</sup>

## 6.10 Prescribing Patterns to Avoid

Concurrent mental health challenges are common among people with AUD. The most commonly reported concurrent mental health disorders are major depressive disorder (15.6%), post-traumatic stress disorder (10.8%), specific phobias (10.6%), and generalized anxiety disorder (7.1%).<sup>627</sup> Globally, people with AUD are frequently prescribed psychoactive medications that are not indicated for AUD treatment, including antidepressants (in 19–59% of patients), antipsychotic medications (9–48%), and benzodiazepines (2–27%).<sup>35</sup> However, a body of literature suggests that even in the presence of concurrent mental disorders, these medications may be ineffective or potentially harmful with respect to alcohol-related and mental health outcomes for some individuals with AUD.<sup>628-630</sup>

It can be challenging to diagnose concurrent disorders due to significant overlap between the biological effects of alcohol use and the symptoms of independent DSM-5-TR diagnoses.<sup>631</sup> Furthermore, depression and anxiety symptoms can result from the neurochemical effects of heavy alcohol use and withdrawal, as well as from the social consequences (e.g., financial instability) that can come with AUD. In turn, mood-related symptoms often improve following AUD treatment<sup>632,633</sup> or a 2–4 week period of abstinence from alcohol, particularly for those with an onset of depression or anxiety after the development of AUD.<sup>634-636</sup>

**Diagnosis of AUD should not be considered a barrier to treatment for concurrent mental health disorders—both AUD and the mental health condition should be prioritized for treatment with evidence-based interventions.**

**Consultation with a concurrent disorders specialist is advised where available.**  
See [Concurrent Substance Use and Mental Health Disorders](#) for more information on concurrent AUD and mental health disorders.

## 6.10.i SSRIs and Other Serotonergic Antidepressants

Antidepressants, particularly selective serotonin reuptake inhibitors (SSRIs) and other serotonergic antidepressants, are frequently prescribed to people with AUD, with and without concurrent depression or anxiety. This section will review the evidence for prescribing serotonergic antidepressants for AUD in individuals without concurrent depression or anxiety, with concurrent depression or anxiety, and in individuals with co-occurring substance use disorders. The literature search was limited to antidepressants classes primarily used in modern clinical practice<sup>an</sup>; older generation antidepressants (e.g., tricyclic antidepressants, monoamine oxidase inhibitors) were excluded.

### 6.10.i.1 Alcohol Use Disorder Without Concurrent Anxiety or Depression

Research investigating the efficacy of antidepressants for individuals with AUD *without* concurrent mental health disorders has been relatively consistent in its findings. A 2005 systematic review and meta-analysis that included evaluation of the efficacy of SSRIs for the treatment of AUD without concurrent depression (N = 5, n = 249) found no significant effect on reduction of alcohol use (OR: 1.83, 95% CI: 0.75 to 4.46).<sup>637</sup> Randomized controlled trials have demonstrated no benefit on alcohol consumption among individuals treated with SSRIs in comparison to placebo.<sup>638,639</sup> Worse alcohol outcomes were demonstrated in a large Canadian RCT (n = 265) which included participants with and without concurrent mental health conditions. As a whole, the group receiving SSRI treatment had a higher number of heavy drinking days (7.60 vs. 4.78 days;  $p = 0.007$ ) and a higher number of drinks per drinking day (5.37 vs. 3.60 drinks;  $p = .03$ ) compared to the placebo

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an The literature search included the following classes of antidepressants: selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, serotonin modulators and stimulators, serotonin antagonists and reuptake inhibitors, norepinephrine reuptake inhibitors, and norepinephrine-dopamine reuptake inhibitors.

group.<sup>640</sup> These findings are consistent with animal research demonstrating that serotonergic antidepressants increase alcohol consumption.<sup>641,642</sup> A number of studies indicate that treatment responsiveness to SSRIs in individuals with AUD and without concurrent depression is moderated by genotype<sup>638,643,644</sup> and age of onset of AUD.<sup>643,644</sup> For example, for individuals in a serotonin transporter genotype subgroup, treatment with sertraline resulted in worse drinking outcomes for those who developed early onset AUD ( $\leq 25$  years of age) ( $p = .011$ ) and improved drinking outcomes for those with late onset AUD ( $> 25$  years of age) ( $p < .001$ ).<sup>643,644</sup> While routine genotyping is not available in clinical care, based on the estimated prevalence of the identified allele in the above study,<sup>643,644</sup> the authors extrapolated that approximately double the number of individuals with AUD on a population level would be adversely affected (i.e., drink more alcohol) than would find benefit if SSRIs were prescribed for the treatment of AUD.<sup>643</sup>

Serotonergic antidepressants are commonly used off-label to treat sleep disturbances in the context of AUD. While one double-blind RCT ( $n = 173$ ) has shown trazodone may have short-term benefits on sleep quality during treatment, following cessation of the medication, alcohol outcomes may worsen, including less improvement in days abstinent compared to placebo and increased number of drinks per drinking day.<sup>466</sup> While the literature is limited and the scope of this guideline does not include reviewing all alternatives for the treatment of insomnia, medications such as gabapentin<sup>537,645</sup> and mirtazapine<sup>645</sup> appear to have better efficacy and safety profiles than serotonergic antidepressants and should be considered.

#### **6.10.i.2 Concurrent Alcohol Use Disorder and Depression**

Several systematic reviews, meta-analyses, and double-blind randomized trials have investigated the efficacy of antidepressants for individuals with concurrent AUD and depression, with results generally finding little benefit, especially when contemporary antidepressants (e.g., SSRIs) are considered.<sup>637,646-649</sup> A 2018 Cochrane Review ( $N = 33$ ,  $n = 2,242$ ; SSRI-specific  $N = 14$ ,  $n = 1,465$ ) found evidence of modest beneficial effect from the use of SSRIs in the treatment of individuals with concurrent AUD and depression in certain outcomes (e.g., number of abstinent participants, drinks per drinking day), but there was no benefit in other relevant outcomes (e.g., rate of abstinent days, heavy drinking

days per week, time to first relapse, depression severity).<sup>646</sup> Systematic reviews and meta-analyses published prior to the Cochrane review found no effect of SSRIs compared to placebo on depression outcomes<sup>637,647</sup> or drinking outcomes.<sup>637</sup> A more recent 2021 meta-analysis (N = 36, n = 2,729; SSRI-specific N = 12, n = 611) had low confidence that SSRIs improved alcohol-related outcomes post-intervention. In this analysis, there was a trend for SSRIs to increase the risk of adverse events (OR: 2.21, 95% CI: 0.94 to 5.16;  $p = .07$ , moderate confidence),<sup>648</sup> while the 2018 Cochrane Review found no difference in adverse events between SSRIs and placebo.<sup>646</sup> In a large Canadian trial (n = 265) of individuals with AUD, 60% of whom had concurrent depression, SSRI treatment resulted in a higher number of heavy drinking days (7.60 vs. 4.78 days;  $p = 0.007$ ) and higher number of drinks per drinking day (5.37 vs. 3.60 drinks;  $p = .03$ ) compared to placebo.<sup>640</sup> All participants received weekly individual and group therapy over 12 weeks and showed significant improvements in depression and anxiety symptoms; however, there were no differences between SSRI and placebo. The authors concluded that SSRIs may be contraindicated in early AUD recovery prior to abstinence. The study sample included considerable comorbidities with 31% of the sample reporting past suicidal ideation and 18% reporting a past suicide attempt. For youth with concurrent AUD and depression, 2 very small double-blind RCTs comparing treatment with SSRIs versus placebo found no benefit of SSRI therapy in either depression or alcohol use outcomes.<sup>650,651</sup>

The studies described above focused on SSRIs alone, not in conjunction with AUD pharmacotherapy treatment. Studies investigating SSRIs in combination with naltrexone have been mixed and inconclusive: combination treatment has been found to be more effective than naltrexone alone<sup>652</sup> or no better than placebo.<sup>653</sup> One study using a variety of antidepressants also found that combination treatment was not better than naltrexone alone.<sup>654</sup>

The evidence summary presented above is aligned with the recommendation published in 2014 and last updated in 2021 by [Choosing Wisely Canada](#), a campaign focused on reducing unnecessary tests and treatments, which recommends against routine prescribing of antidepressants as first-line treatment for depression concurrent with active AUD.<sup>655</sup> This guideline committee has noted the importance of providing comprehensive, non-stigmatizing treatment to individuals with AUD and concurrent depression that encompasses a range of



evidence-based pharmacological and non-pharmacological approaches including psychotherapy. For example, cognitive behavioural therapy (CBT) has shown efficacy for reducing alcohol consumption and depressive symptoms in patients with AUD and concurrent depression<sup>649</sup> (see [Ongoing Care—Psychosocial Treatment Interventions](#)). Specialty consultation is advised, where available.

### **6.10.i.3 Concurrent Alcohol Use Disorder and Anxiety-related Disorder**

For individuals with concurrent AUD and an anxiety-related disorder (generalized anxiety disorder, social anxiety disorder, obsessive-compulsive disorder, panic disorder, post-traumatic stress disorder [PTSD], specific phobia), a 2015 Cochrane review (N = 5, n = 290) assessing the effects of pharmacotherapy found limited and inconclusive evidence.<sup>656</sup> There was very low quality evidence for an effect of paroxetine on provider ratings of patient improvement (assessed by the Clinical Global Impressions—Improvement scale) compared to placebo, but no evidence of efficacy of SSRIs for reducing anxiety symptom severity or improving alcohol use outcomes. There is a growing literature on the interaction between serotonergic antidepressants and psychosocial treatments, with some evidence suggesting that serotonergic antidepressants may decrease the efficacy of CBT.<sup>657</sup> More research is needed to determine the effects of combining serotonergic antidepressants with other interventions.

### **6.10.i.4 Co-occurring Substance Use and Antidepressants**

Co-occurring substance use is common among people with AUD, with between 15% and 25% of individuals with AUD meeting diagnostic criteria for another substance use disorder (i.e., tobacco, opioids, cocaine, and other illicit drugs) in the past year.<sup>658-660</sup> Overall, serotonergic antidepressants have been ineffective in treating symptoms of other substance use disorders, similar to the alcohol literature, with some randomized trials suggesting they may actually increase rates of cannabis,<sup>661</sup> tobacco,<sup>662</sup> cocaine,<sup>663</sup> and methamphetamine<sup>664</sup> use. These increased rates of substance use have been attributed to the role of the serotonergic system dysregulation in substance use disorders and genetic interactions with serotonergic drugs,<sup>665-667</sup> as well as the potential role of SSRIs in disinhibition and increased craving.<sup>668-671</sup>

### 6.10.i.5 Summary of Antidepressants

Based on the evidence showing a lack of benefit<sup>637</sup> and potential for worsened drinking outcomes,<sup>466,643</sup> serotonergic antidepressants should not be prescribed as treatment for AUD in individuals without concurrent anxiety or depression. Additionally, given the lack of high-quality evidence supporting the effectiveness of SSRIs for those with concurrent AUD and depression,<sup>468,646</sup> a potential higher risk of adverse events<sup>648</sup> including worsening drinking outcomes, and research demonstrating a rapid reduction of depressive symptoms following a period of abstinence from alcohol use,<sup>635,636</sup> SSRIs are not recommended for individuals with concurrent AUD and depression. If SSRIs are considered, clinicians should monitor patients for adverse events including worsening AUD outcomes. Similarly, SSRIs are not recommended for treatment of AUD with a concurrent anxiety disorder given the lack of efficacy on either anxiety symptom severity or alcohol use outcomes.<sup>656</sup> Furthermore, scrutiny of the antidepressant literature<sup>ao</sup> has raised concerns about industry influence and the under-reporting of adverse effects.<sup>672</sup>

There is insufficient evidence to develop guidance on SSRI use in individuals in remission from AUD. If SSRIs are used for treatment of depression or anxiety in patients in remission from AUD, clinicians are encouraged to counsel patients on possible adverse effects including increased craving or use of alcohol, follow patient responses closely, and consult or refer to a specialist where available and when needed.

### 6.10.ii Antipsychotics

Clinical experience of the committee suggests that certain antipsychotics are regularly prescribed off-label to individuals with AUD who have not been diagnosed with a psychotic disorder, despite a lack of evidence to support their use in this population. A 2013 meta-analysis (N = 13, n = 1,593) examining the use of antipsychotic monotherapy in individuals who have AUD without concurrent

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ao A 2015 article identified 185 meta-analyses evaluating antidepressants for depression published between 2007 and 2014 and found that these were often produced by industry employees (29%) or authors with industry ties (79%), and results were aligned with sponsor interests.<sup>672</sup>

major psychiatric disorders (e.g., schizophrenia, bipolar disorder) found that antipsychotics did not differ from placebo and, for some alcohol outcomes, performed worse than placebo.<sup>673</sup> Antipsychotics did not differ from placebo in terms of cravings, time to first alcohol consumption, treatment adherence, or preventing relapse, although flupentixol decanoate in particular had higher relapse rates to alcohol use compared to placebo (RR = 1.14, 95% CI: 1.03 to 1.27;  $p = .01$ ). Antipsychotics were found to be inferior to placebo in terms of abstinence or drinking days (SMD = 0.17, 95% CI: 0.01 to 0.33;  $p = .04$ ); however, this finding was driven by one study of flupentixol decanoate and there was no significant difference between antipsychotics and placebo when this study was removed from analysis.

There is mixed evidence from individual RCTs on the effects of prescribing antipsychotics to individuals with AUD. Several RCTs suggest antipsychotics may increase or have no effect on alcohol use in individuals with AUD,<sup>674-678</sup> and some studies suggest that antipsychotics may increase rates of other substance use,<sup>ap</sup> specifically cannabis,<sup>681</sup> tobacco,<sup>682,683</sup> and stimulants.<sup>679,684,685</sup> Other studies show a reduction in alcohol consumption for specific populations,<sup>686-688</sup> including those with lower impulse control,<sup>686,687</sup> concurrent schizophrenia,<sup>689</sup> bipolar disorder,<sup>690</sup> or bipolar disorder concurrent with anxiety disorder.<sup>688</sup> Some studies have investigated the effects on specific dimensions of AUD and found a reduction in drinking cue-induced alcohol craving with olanzapine<sup>691,692</sup> and improved response inhibition with quetiapine<sup>693</sup>; however, it is unclear whether these effects will translate into a reduction in alcohol use or AUD symptoms. A 2018 double-blind, placebo-controlled study ( $n = 90$ ) examining topiramate and aripiprazole versus placebo for the treatment of AUD found that aripiprazole was ineffective for the alcohol-related outcomes analyzed.<sup>694</sup> Furthermore, there are many short- and long-term side effects of antipsychotic use that have been described elsewhere and are relevant to those with AUD,<sup>695</sup> including increased risk of falls and lowering of the seizure threshold.<sup>695,696</sup>

The current evidence does not support the use of antipsychotic medications in

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ap The mechanisms by which antipsychotics may increase substance use are not fully known; however, it has been hypothesized that dopamine receptor antagonism may lead to increased substance use to compensate for reduced levels of dopamine.<sup>679,680</sup>

individuals with AUD outside of treatment for an indicated mental health condition (e.g., schizophrenia). Primary care providers are encouraged to consult with or refer to a specialist to treat concurrent AUD and serious mental health disorders.

### 6.10.iii Benzodiazepines

Clinical experience of the committee and emerging evidence suggest that it is relatively common for individuals with AUD to be prescribed benzodiazepines for ongoing care in an unsafe way, including being prescribed chronic benzodiazepine therapy by clinicians unaware of the risks in this population.<sup>467</sup> For example, in a 2021 observational study of 153 individuals hospitalized in a French inpatient unit for alcohol withdrawal, 75 (49%) reported using benzodiazepines and 43% of those patients consumed benzodiazepines and alcohol in combination.<sup>467</sup> A proportion of the patients using benzodiazepines reported using benzodiazepines other than as prescribed (27 individuals; 36% of patients using benzodiazepines), 89% of whom had a medical prescription for benzodiazepines (24 individuals; 32% of patients who reported using benzodiazepines). Given the average duration of benzodiazepine use (2.5 years) and average of 2 previous alcohol withdrawal attempts, the authors speculate that some patients were initially prescribed benzodiazepines by a specialist for alcohol withdrawal, with a general practitioner then renewing the prescription for chronic use rather than withdrawal.

While benzodiazepines are commonly used for withdrawal management for patients at high risk of severe withdrawal complications, long-term benzodiazepine use is not recommended. The risks and side effects of benzodiazepines increase with duration of use, escalating doses, and when used in combination with other CNS depressants.<sup>325</sup> Using benzodiazepines in combination with other CNS depressants (e.g., alcohol, opioids) can lead to coma, overdose, and death.<sup>697-701</sup> Benzodiazepines have a high potential for non-medical use and dependence; physiological dependence can develop quickly.<sup>326</sup> Short and long-term benzodiazepine use is positively associated with harms such as persistent memory or other neurocognitive deficits,<sup>327-329</sup> motor vehicle collisions,<sup>330,331</sup> increase in severity of anxiety and PTSD,<sup>332</sup> and suicidal thoughts and behaviours.<sup>333</sup>

Additionally, controlled laboratory studies have suggested that benzodiazepine use may have a cross-priming effect that increases motivation for and use of alcohol.<sup>702</sup> Benzodiazepines should only be prescribed as a short-term medication to patients with AUD during withdrawal management, ideally in an inpatient setting, and should not be prescribed as ongoing treatment for AUD. Clinicians should be aware of the risks of long-term benzodiazepine prescribing and should avoid transitioning short courses of benzodiazepines for alcohol withdrawal management into chronic prescriptions. The risks and benefits of benzodiazepines should be discussed with the patient prior to prescribing. See [Pharmacotherapies for Withdrawal Management](#) for more information on benzodiazepines. For patients that have used benzodiazepines for more than 4 weeks for the treatment of AUD or insomnia, clinicians are encouraged to initiate a slow tapering and deprescribing process in accordance with the [Canadian clinical practice guideline](#) and [benzodiazepine deprescribing algorithm](#).

#### 6.10.iv Section Summary and Recommendations

Several commonly used medications, including certain antidepressants, antipsychotic medications, and long-term benzodiazepines, may be ineffective or even potentially harmful for individuals with AUD.

For individuals without concurrent anxiety or depression, moderate quality evidence from a meta-analysis and several RCTs showed no benefit of SSRIs or a potential for worse alcohol use outcomes. For individuals with AUD and concurrent depression, several meta-analyses and trials showed that treatment with SSRIs had no benefit on depression symptoms. However, depression symptoms may improve following a period of abstinence from alcohol use. Low to moderate quality evidence from several meta-analyses suggests a modest beneficial effect of SSRIs on a few drinking outcomes and no effect on all other outcomes studied. For individuals with AUD and concurrent anxiety, moderate quality evidence from a systematic review found no evidence on the efficacy of SSRIs for anxiety or alcohol use. Based on the available evidence, this guideline does not recommend using SSRIs to treat AUD or for patients with a concurrent depressive or anxiety disorder.

For antipsychotics, moderate quality evidence from a meta-analysis showed that antipsychotics performed similarly to or worse than placebo on many alcohol-related outcomes. Data from individual RCTs were mixed, with some indicating increased alcohol and other substance use and some showing reduced alcohol consumption in very specific patient populations. Due to insufficient evidence of effectiveness, this guideline does not recommend prescribing antipsychotics to treat AUD in individuals who do not have an indicated severe and chronic non-alcohol-related mental health condition (e.g., schizophrenia).

Benzodiazepines are often prescribed to patients beyond acute withdrawal management, despite recommendations against long-term benzodiazepine use.<sup>467</sup> Benzodiazepines, when used with alcohol or other CNS depressants (e.g., opioids) may lead to significant harm, including coma, overdose, and death.<sup>697-701</sup> Benzodiazepines have a high potential for dependence and adverse outcomes. This guideline recommends only prescribing benzodiazepines as a short course, fixed-dose prescription to patients during withdrawal management, in closely monitored settings, and not as ongoing treatment for AUD.

**Individuals presenting with symptoms of concurrent disorders should be offered evidence-based interventions to treat the mental health condition as well as AUD. In cases where medications have demonstrated benefit, clinicians should balance the potential benefits and risks of prescribing these medications for each patient and are encouraged to consult or refer to a specialist, where appropriate. Mental health symptoms should be regularly reassessed during initial stages of AUD treatment and persistent mental health symptoms warrant further investigation and regular follow-up.**

Guidance on treating mental health conditions is beyond the scope of this guideline. However, it is emphasized that individuals should be offered or referred to evidence-based treatment for concurrent mental health conditions and expert consultation is advised when available. Clinicians should be aware of the connection between socially constructed factors (e.g., poverty, systemic racism, and housing insecurity) and mental health; the impacts of colonization and systemic oppression on depression and anxiety; as well as the link between trauma and substance use. Treatment plans should be developed with awareness of these factors and aim to mitigate them where possible.

## Recommendation 12

**Adult and youth patients should not be prescribed antipsychotics or SSRI antidepressants for the treatment of AUD.**

**MODERATE** Quality of Evidence

**STRONG** Recommendation

### Remarks

- Randomized controlled trials and systematic reviews investigating SSRIs in individuals with AUD without concurrent depression or anxiety have generally shown that SSRIs are ineffective or may worsen AUD outcomes in some subpopulations with AUD.
- A meta-analysis examining the use of antipsychotics in individuals who have AUD without concurrent major psychiatric disorders (e.g., schizophrenia, bipolar disorder) found no difference or worse alcohol outcomes compared to placebo. Subsequent studies confirmed these findings.
- Given the prevalence of psychoactive medication prescribing to individuals with AUD, alongside the lack of efficacy and potential for avoidable costs, side effects, and other harms, there is significant opportunity for practice change involving greater incorporation of evidence into care.
- The quality of this evidence was rated as moderate based on two systematic reviews and several RCTs of SSRI antidepressants and antipsychotics among people with AUD and without concurrent mental health disorders.
- The strength of this recommendation was rated as strong based on the quality of the evidence base, working group consensus, and known possible costs and harms. It is working group consensus that these medications should only be considered for patients who have an indicated mental health disorder where the medication has clearly demonstrated benefit.

## Recommendation 13

Prescribing SSRI antidepressants is not recommended for adult and youth patients with AUD and a concurrent depressive or anxiety disorder.

**MODERATE** Quality of Evidence

**STRONG** Recommendation

### Remarks

- Meta-analyses and trials demonstrate that SSRIs are generally ineffective for mood and most alcohol use outcomes, with some studies resulting in higher alcohol use, among individuals with AUD and concurrent depression or anxiety.
- Depression and anxiety symptoms among individuals with AUD may improve following a period of abstinence, therefore investigation and follow-up for all diagnoses is required. In cases where mood symptoms do not resolve following cessation of alcohol, evidence-based modalities, including pharmacological and psychosocial treatment options, should be offered for both AUD and the mood disorder. Consultation with or referral to a concurrent disorders specialist is encouraged, where available.
- If SSRIs are considered, clinicians should monitor patients for adverse events including worsening alcohol-related outcomes such as an increase or ongoing heavy drinking.
- The quality of this evidence was rated as moderate based on three systematic reviews or meta-analyses and several RCTs of SSRI antidepressants among people with AUD and concurrent mood and anxiety



## Recommendation 14

**Benzodiazepines should not be prescribed as ongoing treatment for AUD.**

HIGH Quality of Evidence

STRONG Recommendation

### Remarks

- Clinicians should be aware of the risks of long-term benzodiazepine prescribing, and should avoid transitioning short-term benzodiazepine prescribing for alcohol withdrawal management into long-term prescriptions.
- While benzodiazepines are commonly used for withdrawal management, this practice should be restricted to patients at high risk of severe withdrawal complications. Long-term benzodiazepine use is not recommended as the risks and side effects of benzodiazepines increase with duration of use.
- Benzodiazepine use has a high potential for dependence and other harms including persistent memory or other neurocognitive deficits, motor vehicle collisions, increase in severity of anxiety and PTSD, and suicidal thoughts and behaviours. Using benzodiazepines in combination with other CNS depressants can lead to coma, overdose, and death.
- The risks and benefits of benzodiazepines should be discussed with the patient prior to prescribing.
- The quality of evidence for this recommendation was rated as high based on multiple meta-analyses and RCTs showing the harms related to benzodiazepine use, potential for non-medical use, and documentation of the serious adverse effects and events including falls and injuries.
- The strength of this recommendation was rated as strong based on working group consensus and known possible harms of benzodiazepine use among people with and without AUD.

# 7 Community-Based Supports and Programs

## 7.1 Peer Support Groups

Peer-based support groups are widely available, no-cost, community-based meetings that are often recommended as an adjunct to clinical care and management of substance use disorders or as a source of additional peer-based guidance, mentorship, and support in achieving and sustaining recovery and self-defined wellness. Peer support groups are often led by volunteers with lived experience of substance use disorders. While there have been few systematic reviews of the effects of peer-based recovery support services in improving alcohol-related outcomes (i.e., return to alcohol use rates, alcohol consumption), it is recognized that peer-based support has consistently been identified as an important facilitator in helping individuals set goals for, work toward, and maintain recovery from substance use disorders in the research literature<sup>703,704</sup> and by those with lived experience.<sup>705-708</sup> Peer support is also consistent with many Indigenous approaches to healing, which are relational rather than transactional, community-centred, and community-driven.

### 7.1.i Alcoholics Anonymous and 12-Step Programs

A widely recognized and accessible example of a peer support group is Alcoholics Anonymous (AA), an international fellowship of support groups comprised of individuals in recovery, which offers emotional support and a structured “12-step” approach to achieving abstinence. A central concept in AA is that AUD is a spiritual disease, and that recovery is a journey involving belief in a higher power, personal exploration, and acceptance. Some people may not feel comfortable participating in AA for several reasons, including a frequent requirement among peers to be abstinent, services that may be unwelcoming or unsafe for 2S/LGBTQ+ individuals, the religious nature of the program, or feeling a lack of safety in co-ed spaces. Referrals should be made with an understanding of each patient’s identity, goals, and lived experiences. Alcoholics Anonymous groups in some communities provide

dedicated spaces for specific populations (e.g., women, older adults, 2S/LGBTQ+ individuals). For patients whose values do not align with belief in a higher power, secular peer support groups, such as SMART Recovery, are available. Patients should be encouraged to explore a number of different groups to assess fit.

The twelve-step facilitation (TSF) approach is a manualized structured counselling approach in which trained health care providers collaboratively review and discuss the core 12-step principles with their patients, and encourage regular attendance at community-based 12-step meetings for peer support.<sup>709</sup> Twelve-step facilitation was originally designed as an individually-oriented therapy, but it has also been studied as a family-based or group intervention, most often as part of a structured treatment program (e.g., inpatient or intensive outpatient treatment program).<sup>710</sup> A 2020 Cochrane review and meta-analysis (N = 27, n = 10,565) found that clinically delivered and manualized (i.e., the intervention is delivered according to a standardized procedure) TSF and AA may result in higher continuous rates of abstinence (RR = 1.21, 95% CI: 1.03 to 1.43) compared to other psychosocial treatments (e.g., CBT, motivational enhancement therapy) after 12 months. This effect was not observed for non-manualized TSF/AA, which is the more commonly available and accessed format. No difference was found for other outcomes (i.e., percent days abstinent, longest period of abstinence, drinks per drinking day, percentage days heavy drinking, and adverse alcohol-related consequences) between manualized TSF/AA and other psychosocial treatment options. Non-manualized AA/TSF was not found to be more effective than other psychosocial treatment options for the majority of outcomes, with the exception of significantly fewer drinks per drinking day (mean difference [MD] = -1.76, 95% CI: -2.33 to -1.29)—although this result was based on a single study.<sup>711</sup>

Individuals who do benefit from participation in 12-step groups report that factors such as the group dynamic (e.g., feeling a connection to and a sense of belonging and community with others),<sup>712</sup> improved self-awareness,<sup>713-715</sup> an experience of acceptance and empathy from and for others,<sup>716</sup> and developing or strengthening a connection with their spirituality<sup>717,718</sup> were important in starting and maintaining their recovery.

Twelve-step support groups are reported to be most effective at promoting abstinence amongst those who identify with the core philosophy, and who attend

meetings voluntarily on a regular basis,<sup>719</sup> although more research on this topic is needed. Voluntary attendance is of particular importance, as evidence suggests that coerced or mandated treatment may be less effective toward the goal of reducing alcohol or other substance use or achieving abstinence.<sup>720-722</sup> Furthermore, mandating attendance at 12-step groups may be inappropriate for those who do not identify with the spiritual beliefs of the approach, and can harm the relationship between patient and provider and violate the patient's personal autonomy.

### **7.1.ii Self-Management and Recovery Training (SMART Recovery)**

Self-Management and Recovery Training, or SMART Recovery, is a secular alternative to the 12-step model that has rapidly expanded in recent years. The SMART Recovery program was designed to reflect evidence-based practice elements of motivational interviewing, CBT, Rational Emotive Behaviour Therapy, and mindfulness.<sup>723</sup> The “4-point program” of SMART Recovery, which encompasses building motivation, coping with urges, problem solving, and lifestyle balance, provides members with evidence-based tools and peer support to aid in their recovery.<sup>723</sup>

A 2017 systematic review of 12 studies of SMART Recovery programs concluded that while positive effects were found, the lack of RCTs, small sample sizes, and heterogeneity in methods and outcomes assessed across studies prevented drawing conclusions about its effectiveness.<sup>724</sup> To date, only one randomized trial in 2013 has studied the impact of SMART Recovery among individuals with substance use disorders, and it compared in-person SMART meetings to “Overcoming Addictions” (OA), a web-based intervention based on the SMART Recovery program.<sup>725</sup> Individuals with AUD (n = 189) were randomized to receive SMART, OA, or a combination of the two.<sup>725</sup> No differences were found between groups, but at the conclusion of the study there was a significant increase in the percentage of days individuals abstained from alcohol use (44% to 72%;  $p < .001$ ) and a reduction in the number of drinks per drinking day (8.0 to 4.6 drinks;  $p < .001$ ) for all study participants.<sup>725</sup> There is a need for further research, specifically well-designed clinical trials, to better establish the effectiveness of SMART Recovery and other peer support groups in preventing return to alcohol use and reducing alcohol consumption and related harms.

### 7.1.iii Making Informed Referrals to Peer Support Groups

Several studies have found that active referral and encouragement from a clinician or a peer support worker during initial stages of treatment increases the likelihood that patients will attend community-based peer support meetings.<sup>726-729</sup> For example, a 2012 RCT (n = 151) compared active referral from a clinician, active referral from a peer, or information only about local 12-step groups among individuals undergoing inpatient withdrawal management for substances, including alcohol. The study found that active referrals significantly increased attendance rates at meetings during and after withdrawal management (post discharge attendance rates: peer referral 64%, clinician referral 48%, information only 33%), although there were no differences between groups in abstinence rates (44%, 41%, and 36%, respectively).<sup>729</sup> This study highlights the importance of clinicians adopting an active, informed, and encouraging role in referring patients to peer support groups and other community-based services that align with patient goals and preferences. Providing information and encouragement may be particularly helpful for patients and families who may have little to no experience in navigating the AUD treatment system. Involving peer support workers or navigators as part of a clinical care team may also be a valuable strategy for facilitating patient access and engagement.<sup>704</sup>

If a patient identifies incompatibilities between their personal belief systems and the core philosophies of a peer support group as barriers to their participation, alternative options can be provided where available. Clinicians should discuss with their patient if participation in a particular group may better support the patient's treatment goals. For example, some individuals may prefer peer support groups with a secular mandate (e.g., SMART Recovery, LifeRing Secular Recovery), or groups designed for specific populations that reflect their shared lived experiences and provide a sense of safety (e.g., 2S/LGBTQ+ individuals, youth, Indigenous peoples, individuals with concurrent mental health issues). Some women report higher affiliation with and may prefer to attend women-only meetings or groups like the 16-step program based on their perception of enhanced support, safety, and comfort.<sup>730,731</sup> Some individuals may also prefer one-to-one peer support rather than a group setting.

Access to in-person meetings for other (non-12-step) peer support groups may be limited outside of urban centres, although several peer support groups do have online or "virtual" meetings.

## 7.1.iv Section Summary and Recommendation

There is a paucity of high-quality RCTs, systematic reviews, or meta-analyses on the effectiveness of peer support groups among individuals with AUD.

However, it is recognized that some individuals may benefit from or express an interest in accessing peer-based support, guidance, and mentorship, which are core components of many peer-support programs, to navigate the challenges in living with AUD and support an individual's goals of achieving abstinence.<sup>703,704,732</sup>

### Recommendation 15

**Adults and youth with mild to severe AUD should be offered information about and referrals to peer-support groups and other recovery-oriented services in the community.**

**MODERATE** Quality of Evidence

**STRONG** Recommendation

#### Remarks

- Primary care providers should be aware of peer-support groups that are active locally and online, including groups for specific populations (e.g., women, 2S/LGBTQ+, youth, concurrent disorders, etc.), and services for families.
- Primary care providers and care teams should offer information and support voluntary participation in peer-support groups. If patients express interest, encourage patients to attend manualized, structured peer-support groups (e.g., manualized TSF/AA), rather than non-manualized groups.
- Coerced attendance is less effective than voluntary attendance, can harm patient-provider relationships, and violates the patient's personal autonomy. Clinicians and care teams should not support practices that coerce individuals to attend peer-support groups (e.g., as a condition of employment).
- The primary care clinician or care team should continue to play an active role after connecting individuals to peer support groups by checking in on their experiences and overall satisfaction and encouraging regular attendance if the patient is benefitting.
- While there is limited research on peer-based supports for AUD, the quality of evidence for this recommendation was rated as moderate based on the few meta-analyses and randomized clinical trials that have demonstrated small to null benefits for alcohol-related outcomes. Further research could potentially lead to differing results.
- The strength of this recommendation was rated as strong based on the quality of evidence, working group consensus, cost-effectiveness, and the benefits of peer support groups compared to the low risks of adverse consequences.

## 7.2 Community-based Treatment and Recovery Programs

There are a number of recovery-oriented programs and services available that can be beneficial to some patients with AUD. As many of these programs offer a comprehensive range of services, several of which have been reviewed in other sections (e.g., pharmacotherapy, psychosocial treatment interventions, peer-based support) this guideline does not make an explicit recommendation on this topic. However, it is recognized that some patients may benefit from or be interested in accessing more structured treatment and support programs. To support informed decision-making, clinicians should be aware of recovery-oriented programs in their communities, and able to connect patients and families with these resources as required. A brief evidence review of intensive outpatient programs, inpatient treatment, and supportive recovery housing is included below to support the shared decision-making process between health care providers and patients.

### 7.2.i Intensive Outpatient Programs

Intensive outpatient programs (IOP) are ambulatory programs for individuals with substance use disorders who do not require 24-hour care, but do require more support than standard outpatient care. Intensive outpatient programs can also provide an intermediate level of support for individuals recently discharged from inpatient treatment programs. The structure and services provided by these programs vary depending on the setting (e.g., hospital, inpatient treatment, community-based public and private treatment centres) and staffing model (e.g., medical or non-medical personnel). Programs generally offer several hours of structured programming per day, and core services may include individual, group, or family therapy; connecting clients with social supports; life skills and vocational training; peer-support group meetings; therapeutic recreational activities; and developing coping skills and strategies to prevent relapse.

Three clinical trials that randomized clients to an IOP or inpatient treatment found that cumulative days abstinent, alcohol use, and alcohol-related problem scores did not differ significantly between service settings, suggesting that they are similarly effective.<sup>733-735</sup> There were some methodological flaws in these trials, including small sample sizes, non-equivalent groups, single-site studies,

selection bias, and lack of appropriate controls. Intensive outpatient programs may have advantages for some individuals with AUD who would benefit from an intermediate level of support, the ability to develop and practice new skills and strategies while living in the community, and continuity of care for a longer duration. It is noted that standardization of core services offered in IOPs could aid in future comparative effectiveness research and help improve quality and effectiveness of programming.

## 7.2.ii Bed-based Treatment Programs

Bed-based treatment facilities provide a 24-hour, substance-free environment for individuals with alcohol and other substance use disorders. These programs vary in the types of services and treatment models employed, but all typically include core services such as individual and group counselling, life skills training, and peer support groups. Some programs may also include more tailored services, such as vocational training, medical and mental health services, couples/family counselling, and nutritional counselling. Some also offer aftercare services to patients upon program completion, ranging from follow-up counselling, and supportive recovery housing, to IOPs.

Evaluating the effectiveness of bed-based treatment in comparison to other treatment modalities has proven to be methodologically challenging and is an area that has been under-researched.<sup>736</sup> Although a small number of RCTs and other research studies have been conducted, most have not employed a rigorous experimental design and significant methodological limitations have been noted, such as a lack of adequate controls and comparator groups; over-reliance on retrospective, quasi-experimental, and pre-post methods; selection bias; limited generalizability due to setting, study population, and inclusion/exclusion criteria; and heterogeneity in treatment types and outcomes assessed.<sup>736</sup> Additionally, due to ethical concerns associated with randomizing patients to a comparator group that might not provide a sufficient level of care for a patient's needs (e.g., no treatment, outpatient care), several trials excluded participants with moderate to severe AUD and concurrent conditions, to ensure that all study participants received treatment that was clinically appropriate.<sup>736</sup>



In this context, while several systematic reviews have concluded there is low to moderate quality evidence that bed-based treatment programs are effective for reducing substance use and improving health, mental health, social and criminal justice-related outcomes among program participants, there is insufficient evidence that inpatient treatment programs are more effective than other treatment approaches, including outpatient management.<sup>736-740</sup> Nonetheless, research has identified specific patient populations that may benefit from the more structured treatment environment provided in an inpatient care setting (see [Box 9](#)).<sup>737,741,742</sup> The American Society of Addiction Medicine (ASAM) has published criteria to consider for placement, continued stay, transfer, or discharge of patients with substance use disorder and concurrent conditions (previously known as the ASAM Placement Criteria). The criteria can be found on the [ASAM website](#).

*Box 9. Considerations for Referral to Inpatient or Bed-Based Treatment Program*

- Individuals who have not benefited from multiple previous treatment attempts
- Individuals with co-occurring substance use or mental health disorders
  - Before referring a patient to an inpatient treatment program, clinicians should ensure the treatment facility has capacity (e.g., staffing, medications, beds), has appropriately-trained health care providers, and accepts patients with co-occurring substance use or mental health disorders
- Individuals with concurrent medical conditions
  - Before referring a patient to an inpatient treatment program, clinicians should ensure the treatment facility has capacity (e.g., staffing, medications, beds), has appropriately-trained health care providers, and accepts patients with co-occurring medical conditions
- Individuals in a social environment or circumstances that do not support patient-identified treatment goals
- Pregnant individuals who require more intensive medical care and support to improve pregnancy outcomes
- Indigenous people may be interested in accessing bed-based treatment programs that are grounded in Indigenous values and worldviews that offer cultural practices (e.g., sharing circles, smudging) and tailored programming. For example, the [National Native Alcohol and Drug Abuse Program](#) offers treatment centres across Canada that are overseen by Indigenous communities and embed Indigenous healing and culture into inpatient and outpatient treatment programs.
- Consider referring individuals to regulated or licensed facilities, where appropriate and applicable. Note that some culturally-based facilities may not be regulated or licensed; however, these facilities may be the most appropriate facilities for individuals who are interested in culturally-based treatment programs.

### 7.2.iii Supportive Recovery Housing

Supportive recovery housing (i.e., stabilization and transitional living residences, assisted living residences) is a direct support service that provides individuals with substance use disorders (including alcohol) or mental health and co-occurring substance use disorders with safe, typically substance-free accommodation. Supportive recovery housing is time-limited or transitional, not permanent, housing and is often offered to individuals who have completed inpatient treatment as part of a stepped approach to returning to the community. Services offered to residents are generally non-medical and may include a combination of peer coaching or mentoring, group work, and structured activities (e.g., therapeutic recreational activities), with a focus on education and life-skills training to support reintegration with the community.

Very few controlled studies have evaluated the effectiveness of supportive recovery housing for improving substance-related outcomes. Two RCTs that compared supportive recovery housing to usual aftercare (e.g., individual or group counselling, 12-step) reported that individuals residing in supportive recovery housing had reduced substance use and improved employment and criminal justice outcomes compared to individuals in the usual aftercare group.<sup>743,744</sup> However, both trials had methodological limitations, including selection bias, non-equivalent groups, small sample sizes, single-site evaluations, and lack of appropriate statistical controls, which limits ability to draw meaningful conclusions from these results.<sup>745</sup> There is a need for more rigorous research in this area, not only to assess comparative effectiveness of this service option, but also to establish quality standards and best practices for supportive recovery housing programs to optimize patient health outcomes.

## 7.3 Psychosocial Support Services

Given that the social determinants of health play a pivotal role in the overarching health and well-being of individuals, clinicians should offer to connect patients with services that support and attend to patients' needs in these areas. Providing patients with referrals to community-based support services may be helpful in supporting overall recovery by improving an individual's psychosocial

circumstances and other survival needs. Although no systematic reviews have examined the impact of providing supports for various social needs (e.g., housing support, vocational and skills training, social supports, financial assistance) in the context of AUD, studies have demonstrated that providing access to housing and meeting other survival needs can significantly enhance AUD treatment outcomes.<sup>746,747</sup> There is likely a benefit to AUD care being offered in the context of interdisciplinary primary care teams that are equipped to address these needs when possible. Where patients have encountered barriers to engagement in care, effective strategies to improve retention in treatment may include intensive case management,<sup>748,749</sup> assertive community outreach teams,<sup>749-751</sup> and peer-based outreach and support services.<sup>703,704</sup>

# 8 Working with Specific Populations

## 8.1 Indigenous Peoples

**A Note on Terminology:** The source material reviewed in this section uses several different terms to describe the Indigenous peoples in what is presently known as settler Canada. Some are legal terms directly tied to the settler Canadian constitution and various acts (e.g., Section 35 of the [Constitution Act, 1982](#); the [Indian Act, R.S.C. 1985](#)). This terminology has been reproduced here for consistency and accuracy.

In Canada, the term **Indigenous peoples** is considered to be inclusive of all the Peoples of Turtle Island<sup>aq</sup> and all their descendants, and includes those that have status<sup>ar</sup> or not, and those who self-identify as Indigenous. It is important to be aware of the diversity that exists between and among Indigenous peoples in settler Canada. Using the name that reflects a specific peoples, community, or Nations, when possible, is preferred over the collective term “Indigenous.”

The term **Aboriginal** originates from Section 35 of the [Constitution Act, 1982](#), wherein the Aboriginal peoples in settler Canada are defined as “Indian, Inuit and Métis Peoples.” This collective term refers to not a single group, but three very different and distinct groups as defined by the Federal Government. The term reflects the legal and social responsibility of the Federal Government to these excludes those who are not formally recognized by the Government of Canada. In the section below, it is used to specify that health data being reported is specific to people who are registered under the [Indian Act, R.S.C. 1985](#).

**First Nations** is the preferred collective term that replaced “Indian” in Section 35 of the [Constitution Act, 1982](#). It refers to Indigenous peoples in settler Canada who are neither Métis nor Inuit. First Nations Peoples can include both status and non-status Indians. Clinicians need to be aware of this distinction when referring to health care benefits, programs, or services that are only accessible to status Indians.

**Inuit Peoples** are Indigenous peoples in northern Canada (Nunavut, Northwest Territories, Quebec, and Labrador).

**Métis Peoples** are a group of distinct Nations among Indigenous peoples in Canada, and have roots in mixed Indigenous and European ancestry. Métis peoples have common descent, history, language, and culture tied to a specific territory. Being of mixed decent in and of itself does not make an individual Métis.

aq Turtle Island refers to the continent of North America in origin stories from certain nations.

ar “Status” is a legal term for a person who is registered as an “Indian” under the Indian Act, or a person who belongs to a First Nation or Indian Band that signed a treaty with the Crown; this can be denoted as “Status, Registered or Treaty Indian” or “Status, Registered, or Treaty First Nations.” This term has origins and connection to colonial policies.

According to the 2021 Census, 1.8 million people in Canada self-identify as Aboriginal, making up 5.0% of the Canadian population, up from 4.9% in 2016.<sup>752</sup> Census data shows that the number of Aboriginal peoples is growing in Canada, though this growth was not as rapid as in years past.<sup>753</sup>

For thousands of years prior to European contact, Indigenous peoples enjoyed good health and wellness due to a lifestyle that was active, enriched by with traditional foods and medicines, and integrated with ceremonial, spiritual, and emotional healing practices. However, the arrival of European settlers had a significant negative impact on the health and wellness of Indigenous peoples. Historical and ongoing impacts of colonization, racial science and eugenics, institutionalized racism, and multigenerational trauma have direct impacts on physical and mental health, as well on the social determinants of health, which has led to disproportionate prevalence of health concerns in Indigenous people. The health and social inequities experienced by Indigenous peoples have created conditions where some individuals use alcohol and other substances to cope with racism, discrimination, poverty, trauma, violence, or other sources of distress in their daily lives.<sup>754,755</sup> Statistics on alcohol use must therefore be interpreted within a broader social framework that acknowledges the role of historical and current discriminatory systems.

Canadian data from 2016 show that a similar proportion of Aboriginal peoples aged 12 and over are abstinent from alcohol (27.4%) in the past 12 months compared to non-Aboriginal Canadians (25.5%).<sup>756</sup> However, the prevalence of heavy drinking, AUD, and alcohol-related harms among Aboriginal peoples who do drink alcohol is significantly higher than in non-Aboriginal Canadians.<sup>756</sup> For example, 25.1% of First Nations peoples reported heavy drinking<sup>as</sup> in the past month, compared to 19.6% of non-Aboriginal Canadians.<sup>756</sup> Nationally, the rate of alcohol-related mortality is estimated to be 5.43 times higher in First Nations men and 10.11 times higher in First Nations women compared to non-Aboriginal counterparts.<sup>95</sup>

Research has highlighted the important role of culturally safe and informed

as Statistics Canada: heavy drinking is defined as five or more drinks on a single occasion at least once a month

approaches to reduce disparities in substance use care for Indigenous populations.<sup>76,757</sup> This guideline strongly recommends that all health care professionals and staff undertake Indigenous cultural safety and cultural humility training to improve their ability to establish safe, positive partnerships with Indigenous patients and families (see [Indigenous Cultural Safety](#)). The [Calls to Action](#) from the [Truth and Reconciliation Commission Reports](#), recommendations in the [In Plain Sight Report](#), and [Calls for Justice](#) from the National Inquiry into Missing and Murdered Indigenous Women and Girls Final Report outline the necessary actions to address the legacy of colonialism in a range of domains including health care. A human rights-based approach is also essential due to Canada's history of discriminatory, unethical, and harmful treatment of Indigenous peoples in the mainstream health care system.<sup>160</sup> In addition to incorporating Indigenous cultural safety and cultural humility in standard medical practice, several principles of providing ethical care to Indigenous peoples have been identified in the literature<sup>758</sup>:

- Respecting the individual and their authority over their own health and healing journey
- Practicing conscious communication, active listening, and paying close attention to how a person responds to questions and conversation, both in their speech and body language, to ensure their comfort and safety
- Using interpreters if fluency in English or French is a barrier to communication
- Involving family members in decision-making, when appropriate, and as key sources of support, and respecting an individual's definition of family, which can include many extended relations

- Recognizing that some individuals may prefer alternative methods for communicating and receiving information about their health—the practice of “offering truth”<sup>at</sup> and honouring a patient’s decision on the type of information they wish to receive and how they wish to receive it may be helpful in this context
- **Practicing non-interference in a patient’s decision-making, unless there has been a clear misunderstanding—strong advice or persuasive language from a person in a position of power (i.e., clinician to patient) can be interpreted as coercive**
- Respecting Indigenous peoples have the inherent and recognized right to access cultural practices as part of their health care

Clinicians who provide care to Indigenous peoples should be familiar with the [Non-Insured Health Benefits](#) program, including eligibility and coverage requirements, and the exceptions and special permissions needed in some cases.

### 8.1.i Access to Cultural Practices

Indigenous approaches to health are holistic, relational, and seek to balance physical, spiritual, mental, and emotional wellness.<sup>93</sup> However, many clinicians who provide substance use care subscribe to a biomedical approach that is disease- and individual-focused—an approach that has been acknowledged as largely incongruent with Indigenous worldviews.<sup>760</sup> Conventional substance use care has been shown to be less effective for, and potentially harmful to Indigenous peoples, with some suggesting this is partially attributable to the lack of cultural practices incorporated into treatment interventions<sup>761</sup> and delivery of care that does not adhere to Indigenous values and worldviews.<sup>93</sup> Moreover, the majority of clinical research on AUD treatment has been conducted in non-

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at The practice of “offering truth” recognizes that a patient may wish to receive little information or as much information as possible about their diagnosis, prognosis, and treatment. A patient’s desired knowledge of their medical condition exists along a continuum and clinicians should ensure they discuss the type of information a patient wants to receive and how the patient wants to receive that information before sharing a diagnosis and beginning treatment.<sup>759</sup>

Indigenous populations, limiting the ability to determine whether recommended interventions are applicable and suitable for people with Indigenous and other cultural backgrounds. The value of using the teachings of Mi'kmaq Elder Albert Marshall's "Two-Eyed Seeing" approach, which respects and integrates the strengths of both Indigenous knowledge and Western medicine,<sup>762</sup> has been increasingly recognized in holistic wellness and substance use care for Indigenous peoples.<sup>760</sup> Further reading on this approach is available [online](#) (see Chapter 5).

There is widespread agreement among Indigenous Elders and healers, as well as researchers, that the inclusion of cultural practices in substance use care is essential to promoting healing for Indigenous peoples.<sup>763,764</sup> Indeed, substance use treatment interventions that incorporate Indigenous cultural practices have been found to improve the physical, mental, emotional, and spiritual health of Indigenous peoples (e.g., reduced substance use, reduced rates of mental health issues, improved relationships, increased participation in cultural practices).<sup>763</sup> Access to traditional Indigenous health care practices can enhance self-determination over health care, which is a key determinant of health for Indigenous individuals and communities.<sup>765</sup> Indigenous patients have an inherent right to access cultural practices as part of their health care, as acknowledged and highlighted by Call to Action #22 of the [Truth and Reconciliation Commission](#), which calls on the health care system to recognize the value of Indigenous cultural practices and to use them in collaboration with Indigenous Elders and healers when delivering care to Indigenous people.<sup>766</sup> In recognition of this, clinicians, care teams, and staff should ensure Indigenous people can access cultural practices as a component of their AUD care:

- Clinicians should inquire with Indigenous people about their interest in including cultural practices as part of their AUD care, while understanding that Indigenous people have differing levels of involvement and interest in cultural practices for historical and personal reasons.
- Some Indigenous people may already be engaged in cultural practices, whereas others may have no interest in accessing cultural practices. In either situation, clinicians should offer support to the patient and be aware that the patient's preferences for accessing cultural practices may change over time.
- If a patient is already engaged in cultural practices, clinicians should, with the



consent of the patient, work collaboratively with the patient's Elder or healer in care planning.

- Patients who do not have an Elder or healer may be connected to one within the care setting, if available, or in the community.
- Clinicians may also inform patients of any sacred spaces that are available to Indigenous people in the care setting. Any patient requests to access a specific cultural practice or medicine should be satisfied within a timely manner.

A diversity of cultural practices can be integrated into substance use treatment interventions depending on resources, capacity, and expertise, including smudging, storytelling, teachings, fasting, carving, beadwork, land-based activities, pow-wows, traditional foods and medicines, language, talking circles, drumming, singing, community feasts, sweat lodges, and prayer.<sup>760</sup> Clinicians should also be aware of regional and provincial resources available to Indigenous patients and families. In some areas, treatment centres that incorporate Indigenous cultural practices may be available for Indigenous peoples who prefer culturally-based AUD treatment. The Government of Canada publishes a webpage with a list of [substance use treatment centres for First Nations and Inuit](#). Health authorities, hospitals, and First Nations Treatment Centres may be able to provide or connect patients to Indigenous patient navigators, interpreters, or sacred spaces. Indigenous patient navigators or liaisons may support patients and their families, clinicians, and care teams by<sup>767,768</sup>:

- Connecting patients with Elders and other cultural supports
- Facilitating communication between patient and care teams
- Assisting with referrals within a health authority and to community organizations, acting as an advocate on the patient's behalf
- Liaising with Indigenous communities and organizations
- Arranging for translators
- Guiding patients through the health care system
- When patients are eligible, connecting patients to Non-Insured Health Benefits for medical and other coverage

Clinicians, care teams, and staff should do their own learning first, and where appropriate, seek support from the Indigenous health team within their local health authority when providing care to Indigenous patients, if available. Individual primary care providers may not have access to these resources and should instead ask their Indigenous patients how they can best support their patient's use of cultural practices during their patient's care. This may include connecting the patient to cultural supports in the community, working in partnership with the patient's Elder or healer, or providing a space for the patient to engage in cultural practices. Clinicians may also choose to have the Four Sacred Medicines that are common to most First Nations in Canada (cedar, sage, sweetgrass, and tobacco) freely available to Indigenous patients in their clinic.

For more information on Indigenous cultural practices in clinical settings, clinicians can refer to [Substance Use Treatment and Land-Based Healing – Task Group on Mental Wellness](#), Vancouver Coastal Health's [Aboriginal Cultural Practices: A Guide for Physicians and Allied Health Professionals Working at Vancouver Coastal Health](#), the Toronto Regional Indigenous Cancer Program's [Supporting and Enabling Indigenous Ceremonial Practices within Healthcare Institutions – Wise Practices Guideline](#), [resources](#) from the National Collaborating Centre for Indigenous Health, and the Society of Obstetricians and Gynaecologists of Canada's (SOGC) [Consensus Guideline for Health Professionals Working With First Nations, Inuit, and Métis](#).<sup>183</sup> [Friendship Centres](#) are located across Canada and offer community and cultural practices to Indigenous people. Please see [Indigenous Cultural Safety](#) for further guidance on providing culturally safe care.

## 8.2 Sex and Gender

Sex and gender<sup>au</sup> are key social determinants of health, and they influence the physiological and psychosocial aspects of many health experiences and conditions, including substance use disorders.<sup>769</sup> Yet, the influence of sex and gender on alcohol use and related harms is often overlooked.<sup>769</sup>

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au Sex generally refers to the classification of a person as male, female, or intersex at birth, usually based on the appearance of their external anatomy, whereas gender refers to one's internal, deeply held sense of their gender, which may or may not align with the sex they were assigned at birth.

## 8.2.i Sex Assigned at Birth and Alcohol Use

How bodies process alcohol can differ according to one's sex assigned at birth. Yet, because sex-based differences only have a small impact on lifetime risk of death,<sup>8</sup> Canada has followed the global trend to not differentiate between males, females, and intersex people when formulating guidance for weekly alcohol consumption.<sup>8</sup> However, above low levels of consumption, lifetime risk of health harms increases more steeply for people assigned female at birth.<sup>8</sup> Further, some studies suggest that people assigned female at birth are more susceptible to the effects of alcohol partly due to differences in average body weight, water content, and levels of enzymes that break down alcohol.<sup>770</sup> Thus, with increasing alcohol intake, the risk of developing a range of alcohol-related conditions, including stroke, diabetes, and liver disease, increases more rapidly for people assigned female at birth.<sup>770-772</sup> The ways that gender-affirming hormone therapy may impact alcohol metabolism is not well known at this point.

## 8.2.ii Gender Socialization and Alcohol Use

Drinking behaviours and consequences are influenced by socialization<sup>av</sup>, cultural perceptions, norms, and systems of power related to gender. For example, research comparing boys and girls has suggested that substance use (alcohol use, smoking, and marijuana use) is more prevalent among girls than boys during early adolescence<sup>773</sup> and that girls are more likely to use alcohol and other substances to manage negative emotions (e.g., depression).<sup>774,775</sup> In men, traditional perceptions of masculinity have also been associated with the motivation to consume alcohol and corresponding alcohol-related problems, as well as alcohol-related risk-taking behaviours.<sup>776,777</sup> Another issue is that socio-cultural norms related to gender and gendered power relations can influence whether and how people utilize harm reduction strategies in contexts of alcohol use, such as limiting number of drinks, switching from alcoholic drinks to non-alcoholic alternatives, or having a designated driver, likely due to increased social pressure for risky behaviour.<sup>778</sup>

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av Gender socialization is the process by which society transmits both implicit and explicit messages about the meaning of one's gender in a broader societal context.

Research has also revealed correlations between gender and substance use treatment access and outcomes. For younger women with AUD, barriers to treatment have been recognized and are worse when adding intersections between gender inequality, stigma, and poverty.<sup>779</sup> Health care providers are less likely to refer women than men to outpatient or inpatient alcohol treatment programs, even though research shows there are no differences between men and women in treatment retention or completion rates.<sup>780</sup> Additionally, when they do seek care, women and other people who use alcohol while pregnant or parenting can face distinct challenges, such as judgment, stigma, and more paternalistic or punitive approaches to care.<sup>781,782</sup>

The impact of gender-specific experiences and biases on alcohol use and related harms, including AUD, underscore the importance of sex/gender-informed and gender-inclusive care. The Centre of Excellence in Women’s Health has several resources available through their [Trauma Gender Substance Use Project](#), including a [Gender-Informed Approaches to Substance Use Resource List](#) and the [New Terrain](#) toolkit<sup>78</sup> to support integration of trauma-informed, gender-responsive, and gender-transformative approaches in clinical practice. Clinicians and care teams should be familiar with and offer patients the option of gender-specific substance use treatment and support services in their communities, if available and as appropriate. Women-only settings or women-specific treatment services may improve outcomes for women with AUD.<sup>783</sup>

## 8.3 2S/LGBTQ+ Populations

Two-Spirit<sup>aw</sup>, lesbian, gay, bisexual, trans, queer, and other sexual and gender minority (2S/LGBTQ+) individuals experience health and health care access inequities stemming from social prejudice and discrimination, internalized stigma, and lack of clinician competencies for providing inclusive and affirming care, including in the context of substance use care.<sup>784,785</sup> For example, persisting

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aw Two-Spirit is a term used by some Indigenous communities on Turtle Island to describe people with diverse gender identities, gender expressions, gender roles, and sexual orientations. Two-spirit people have historically been highly respected and honored members of community for their balanced experience, knowledge, and practice. Definition borrowed and lightly adapted from Qmunity’s [“Queer Glossary: A to Q Terminology”](#)

cisheteronormative and often stigmatizing practices in the health system can contribute to trans individuals being or feeling unsafe in health care settings and can delay accessing care. Research consistently identifies that 2S/LGBTQ+ people have disproportionately high rates of substance use,<sup>786-788</sup> and access care after developing more complex substance-related problems<sup>782,789</sup> and greater physical and mental health care needs.<sup>790,791</sup> High-risk alcohol use and alcohol-related harms are reported at increased rates in both adults<sup>792-794</sup> and youth<sup>795,796</sup> who identify as 2S/LGBTQ+ compared to cisgender, heterosexual individuals. It is important to note that the higher prevalence of substance use and substance use disorders in 2S/LGBTQ+ communities is likely attributed to the need to cope with the toll of systemic discrimination and stigmatization<sup>797-799</sup> and not a higher inherent risk. Suggested explanations for these inequities include the stress and internalized stigma of being in a minority group, dealing with social prejudice and discrimination, and gaps in availability of 2S/LGBTQ+-affirming and -inclusive health care.<sup>800,801</sup> The sociocultural context of alcohol use in 2S/LGBTQ+ communities may also be a factor in substance use rates and patterns.<sup>802</sup> Alcohol use has historically been a part of some 2S/LGBTQ+ subcultures,<sup>802</sup> and licenced bars, clubs, and restaurants have traditionally been places where some 2S/LGBTQ+ people have felt comfortable socializing together without fear of stigma from the wider society.<sup>801</sup> It is important for clinicians to note that 2S/LGBTQ+ patients should not be treated as a monolith, and individuals and communities will have varying risks and substance use patterns.

Strategies for working with 2S/LGBTQ+ individuals in the context of substance/alcohol use care, and in general, include a non-judgmental approach, active demonstration of awareness of and sensitivity toward 2S/LGBTQ+ issues, reinforcement of confidentiality, and using open-ended questions about sexuality and gender and avoiding assumptions. Further, clinicians should actively communicate that services are available for 2S/LGBTQ+ patients, build relationships with organizations serving diverse marginalized communities, and use inclusive language in forms and clinical materials, as well as during appointments.<sup>800</sup> Although substance use disorder treatment for 2S/LGBTQ+ individuals is similar to treatment for other populations, additional factors must be considered, including asking about and affirming the patient's feelings about their sexual and gender identities and the impacts of stigma and discrimination in their lives,<sup>803</sup> including in relation to their substance/alcohol use. Other strategies

include respecting that identities are fluid and tailoring care accordingly; mirroring the language that your patients use (e.g., to refer to themselves, their relationships, and bodies); not assuming sexual activity levels or motives for substance use; and being affirming, while recognizing the ways that individuals successfully practice harm reduction in their lives. 2S/LGBTQ+ individuals may also have experienced discrimination in the health care system and thus may have difficulty establishing trusting relationships with a health care providers.<sup>803</sup> Prescribers should make themselves aware of local support groups and resources for 2S/LGBTQ+ individuals. Additional information and guidance can be found in the Substance Abuse and Mental Health Services Administration’s publication, [A Provider’s Introduction to Substance Abuse Treatment for Lesbian, Gay, Bisexual, and Transgender Individuals](#).

Clinicians can demonstrate trans awareness and sensitivity by taking actions such as placing trans-inclusive brochures and posters in waiting rooms, asking about gender identity on intake forms (and avoiding conflating gender and sex<sup>ax</sup>),<sup>804</sup> being reflexive and acknowledging personal biases, recognizing an individual’s intersecting identities (e.g., race, disability, gender, sexuality) and how they may compound and impact patients’ experience of health care, and making gender neutral bathrooms available. Trans clients may prefer trans-specific services or hours, and some may prefer services that exclude cis gender men due to past experiences of violence and the sexual harassment (see [Trauma- and Violence-Informed Practice](#)). More information on working with trans, Two-Spirit, and gender diverse patients can be found in Trans Care BC’s [Gender-affirming Care for Trans, Two-Spirit, and Gender Diverse Patients in BC: A Primary Care Toolkit](#), Sherbourne Health [Guidelines for Gender-Affirming Primary Care With Trans and Non-Binary Patients](#),<sup>805</sup> [Skipping Stone](#) resources for youth, adults, and families across Alberta, and the [Canadian Professional Association for Transgender Health](#).

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ax Sex generally refers to the classification of a person as male, female, or intersex at birth, usually based on the appearance of their external anatomy, whereas gender refers to one’s internal, deeply held sense of their gender, which may or may not align with the sex they were assigned at birth. A person’s sex should not be assumed to match their gender, for example, that a person will have specific genitalia or reproductive anatomy based on their gender identity.

## 8.4 Youth

Abbreviated evidence-based guidance for screening, diagnosis, brief intervention, withdrawal management, and AUD pharmacotherapy in youth has been included in this guideline where the evidence is available. This guideline defines adolescents as individuals aged 11–17 years, young adults as individuals aged 18–25 years, and youth as individuals aged 11–25 years (i.e., inclusive of adolescent and young adult age categories). “Youth” is a fluid age category and service providers in the community may use different definitions; clinicians should confirm that a patient is within the age range served by a particular program before making a referral. Further, research studies also use different definitions and age categories for youth; as such, age ranges and definitions used by study authors are reported in the evidence review.

The lack of tailored, age-appropriate approaches to and options for substance use care have consistently been cited as barriers to engaging youth in treatment.<sup>806,807</sup> Another contributor to low engagement is that youth with AUD may not perceive a need for formal supports or they feel they can handle the problem on their own and may not seek alcohol treatment services of their own accord.<sup>808</sup>

Strategies that primary care clinicians and care teams can use to improve retention and engagement in care in youth include<sup>118,452,809-815</sup>:

- emphasizing confidentiality with and across services
- including family members and other caregivers (e.g., trusted Elders, teachers, outreach workers, counsellors, as well as friends and romantic partners) in care when appropriate
- fostering development of longitudinal therapeutic relationships
- offering a full scope of pharmacotherapy when indicated, providing referrals to youth-oriented psychosocial treatment interventions and supports
- ensuring treatment timelines are adequately discussed with youth and that treatment is provided without a pre-determined end date
- offering harm reduction strategies
- developing a treatment plan that is transparent, contextually relevant, and responsive to their lived experiences
- including peer support staff or referrals to peer support services in the community

Determining youth capacity to consent to treatment is often complex and should be approached with tremendous sensitivity.<sup>816</sup> Capacity to consent for youth is determined in most provinces based on the capacity to fully understand the treatment and possible consequences of treatment and the consequences of not receiving treatment. In two provinces, consent is based on age: in Quebec, the age of consent is 14 years and older<sup>817</sup> and in New Brunswick, the age of consent is 16 unless two medical practitioners are in agreement that the individual is capable of consenting and that the medical procedure in question is in the patient's best interest.<sup>818</sup> Informed consent and discussion of rationale for treatment should be documented, and the limits of confidentiality should be discussed (for example, duty to report). A patient under the legal age of majority seeking treatment who is determined able to understand the treatment and give consent does not require parental permission or notification. However, this guideline recommends the inclusion of family members in decision-making processes and care at all levels, when deemed appropriate by patients and their care teams. Clinicians should make every effort to preserve a trusting and supportive relationship with youth patients and foster self-determination. For more information on determining capacity to provide consent in those under the age of majority, refer to guidance from the Canadian Medical Protective Association<sup>817</sup> and Royal College of Physicians and Surgeons of Canada.<sup>818</sup> Families or clinicians seeking guidance on the application of involuntary care are referred to the [Canadian Medical Protective Association Medico-legal handbook](#).<sup>819</sup>

Additional information on child and youth mental health issues and services for youth patients and their families can be accessed through BC Children's Hospital's [Kelty Mental Health Centre](#), the Canadian Mental Health Association Ontario [Child and Youth Mental Health](#) webpage, and [Kids Help Phone](#) for kids and youth under 20 years of age.



## 8.5 Pregnant Individuals

Abbreviated evidence-based guidance for screening, diagnosis, brief intervention, withdrawal management, and AUD pharmacotherapy in pregnant patients<sup>ay</sup> has been included in this guideline. For additional clinical guidance on the management of alcohol use during pregnancy and postpartum, clinicians can refer to the [Guideline No. 405: Screening and Counselling for Alcohol Consumption During Pregnancy](#)<sup>41</sup> issued by the Society of Obstetricians and Gynaecologists of Canada and the [BCCSU AUD Pregnancy Supplement](#).

There are no universally accepted standards for safe use of alcohol in pregnancy, and most jurisdictions, including Canada, recommend no alcohol use.<sup>41,371</sup> However, according to the most recent Canadian data (the Maternity Experiences Survey), 10.5% of those surveyed reported that they continued drinking alcohol (frequently or infrequently) after realizing they were pregnant.<sup>820</sup> This is likely an underestimation of the true prevalence of alcohol use in pregnancy, as fear of judgment and stigma can lead to significant under-reporting in this population.<sup>41,820</sup> Additionally, when women do seek care, those who use alcohol while pregnant or parenting experience disproportionately higher rates of judgment, stigma, and punitive approaches than men in similar circumstances.<sup>781,782</sup>

It is important clinicians are aware that Indigenous and other racialized individuals experience greater discrimination when pregnant and using alcohol, particularly when combined with the intersection of poverty. There is a historic, living, and ongoing legacy in Canada of systemic removal of Indigenous children from their families and communities, first through residential schools and later through the Sixties Scoop. The child welfare system continues to apprehend Indigenous children today at a disproportionate rate,<sup>821</sup> contributing to tremendous negative impacts on Indigenous mothers and parents.<sup>822</sup> Indigenous women report returning to substance use or using stronger substances following child apprehension.<sup>823</sup> It is important clinicians are aware of the unique and intersectional historical, social, and political

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ay While the majority of pregnant individuals identify as women, this term does not reflect the identities and experience of all pregnant people. Gender-neutral language has been used in this section where possible. Respect for individual identities and use of corresponding or chosen pronouns is an important component of patient-centred care.

contexts surrounding substance use and pregnancy for Indigenous parents.<sup>824</sup>

Alcohol is a known teratogen (i.e., a substance that is known to cause congenital malformations or birth defects in the fetus if consumed during pregnancy). Prenatal exposure to alcohol is associated with Fetal Alcohol Spectrum Disorder (FASD), which is a wide range of conditions that can include growth restriction, developmental delay, neurological abnormalities, and cognitive, behavioral, and physical health issues throughout life.<sup>41,369,371,825</sup> Fetal Alcohol Spectrum Disorder is believed to affect approximately 1% of the Canadian population. Research suggests there is a dose-dependent relationship between the amount of alcohol consumed during pregnancy and severity of alcohol-related effects in the child,<sup>826</sup> however, the degree and type of impairment varies considerably from one individual to the next, and with timing and pattern of alcohol use.<sup>827</sup> Treating AUD in pregnancy is important for both the pregnant person and the fetus.

In line with clinical practice guidelines from the Society of Obstetricians and Gynaecologists of Canada,<sup>41</sup> it is recommended that primary care clinicians and care teams advise patients and families that the safest choice is to not consume alcohol during pregnancy. Education, screening, and assessment of alcohol use in pregnancy should be delivered in a balanced and non-judgmental manner to prevent unintended negative consequences, such as loss to care.<sup>41,827</sup> Research has shown that stigma and fear of judgment is a significant barrier to accessing and staying engaged in treatment among pregnant individuals who use substances.<sup>41</sup>

#### Resources related to pregnancy and AUD:

- [The Centre of Excellence for Women's Health](#) has several guides to support clinicians in engaging with pregnant patients and their partners on alcohol use, pregnancy, and prevention of Fetal Alcohol Spectrum Disorder (FASD), including referral information, on their website.
- [The Society of Obstetricians and Gynaecologists of Canada](#) also has information on alcohol use during pregnancy on the website for patients.
- [The Prevention Conversation](#) is an online training program offered by the Canada FASD Research Network for health care and social service professionals that provides knowledge and skills to engage patients/clients in a conversation about alcohol use during pregnancy.
- [The Consensus Statement: Eight Tenets for Enacting the Truth and Reconciliation Commission's Call to Action #33](#) provides guidance for creating community-based, culture-led FASD prevention programs in Indigenous communities.
- [The Provincial Blueprint for a Perinatal Substance Use Continuum of Care](#) provides guidance on care for pregnant and parenting people using substances.

## 8.6 Older Adults

This guideline defines “older adults” as patients aged 65 or older, although it is understood that some age-related conditions may be present in some adults who are younger than 65 and should be managed similarly. Abbreviated evidence-based guidance for screening, diagnosis, brief intervention, withdrawal management, and AUD pharmacotherapy in older adults has been included in this guideline.

According to recent Canadian data, approximately 7.8% of older adults surveyed met the criteria for heavy drinking<sup>az,828</sup> and 0.6% meet the criteria for an AUD.<sup>9</sup> However, under-reporting substance use may be more common in older adults compared to younger counterparts due to stigma and fear of judgment, as well as cognitive and memory deficits that can impact accuracy of self-report.<sup>829,830</sup> Thus, clinicians should approach screening of older adults with patience and sensitivity, while also being mindful of clinical signs of alcohol-related problems.

Clinicians should be aware that older adults are more susceptible to the effects and harms of alcohol than people who are younger.<sup>831</sup> In addition to lowered alcohol tolerance related to reduced activity of gastric and liver enzymes, older adults may also have multiple concurrent conditions that can be exacerbated by alcohol use.<sup>831,832</sup> However, despite increased risks of alcohol-related harms, drinking above low-risk limits and AUD among older adults is frequently overlooked and unrecognized in primary care practice.<sup>831</sup> As with the general population, alcohol use screening should always be included in routine primary care assessments in older adults. The Canadian Coalition for Seniors’ Mental Health (CCSMH) has published lower-risk drinking limits specifically for older adults.<sup>140</sup>

Clinicians should also be aware of potential signs of alcohol-related problems in older adults, including worsening chronic conditions (e.g., hypertension, diabetes, osteoporosis); changes in effectiveness of prescribed medications; increased frequency of injuries (e.g., falls, fractures, burns); onset or worsening of cognitive or psychiatric disorders (e.g., confusion, anxiety, depression, insomnia, memory

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az Statistics Canada: Heavy drinking was defined as males who reported having 5 or more drinks, or females who reported having 4 or more drinks, on one occasion, at least once a month in the past year

loss); increased social isolation or distress; and poor nutrition and hygiene.<sup>833</sup>

Limited data suggest that AUD treatment outcomes among older adults are similar, and in some cases superior, to those observed in younger patient populations.<sup>834</sup> Due to a higher prevalence of concurrent medical conditions and increased susceptibility to severe complications of alcohol withdrawal, older adults may benefit from a higher intensity, more structured approach to care, such as referrals to inpatient withdrawal management, inpatient treatment programs, or intensive outpatient programs.<sup>832</sup> Additionally, as older patients tend to have a higher prevalence of medical conditions and taking multiple medications for chronic disease management, impact on concurrent conditions and potential drug–drug interactions should be carefully reviewed when selecting AUD pharmacotherapies. Further information can be found in the [Canadian Guidelines on Alcohol Use Disorder Among Older Adults](#).

## 8.7 Concurrent Substance Use and Mental Health Disorders

Concurrent substance use disorders and mental health disorders are common, often as a result of the neurobiological effects of substance use (e.g., alcohol’s contribution to depression) as well as the social effects of substance use disorder (e.g., financial instability, interpersonal conflict). In other circumstances, an underlying mental disorder may contribute to substance use (e.g., an individual with post-traumatic stress disorder using alcohol as a coping mechanism) or the concurrent disorders may share a common cause (e.g., adverse childhood experiences, trauma). Canadian data is lacking, but in the U.S., a nationally representative sample of adults reported an estimated 12-month prevalence rate of concurrent substance use and mental health disorders of 43.3%,<sup>630</sup> and that over 50% of individuals with a severe psychiatric illness (e.g., schizophrenia, psychosis) were estimated to have a concurrent substance use disorder.<sup>447</sup> Individuals with concurrent mental health and substance use disorders, including AUD, typically experience more severe substance-related, psychiatric and physical health symptoms, and face higher risk of psychosocial challenges, including unemployment, poverty, food and housing insecurity, and a lack of social support.<sup>628,629</sup> As is emphasized in this guideline, comprehensive medical and psychological management that adequately addresses concurrent physical and

mental health disorders is essential to patient-centred care. Additionally, referrals to psychosocial supports and peer-based services in the community should be routinely offered to address social determinants of health and health inequities experienced by this population.

### 8.7.i Concurrent Alcohol Use and Mental Health Disorders

In a nationally representative survey of adults in the U.S., the most commonly reported concurrent mental health disorders among individuals with AUD were major depression disorder (15.6%), post-traumatic stress disorder (10.8%), specific phobia (10.6%), and generalized anxiety disorder (7.1%).<sup>627</sup>

Differential diagnosis and treatment of concurrent disorders can be challenging due to the significant overlap in the symptoms of mental health and substance use disorders, particularly in the early stages of treatment for substance use disorders. For example, untreated anxiety and depression may lead to the development of AUD if individuals use alcohol over an extended time period to relieve their symptoms.<sup>628,629</sup> Conversely, anxiety and depression can also be symptoms of alcohol withdrawal or AUD.<sup>628,835</sup> Thus, assessment of concurrent disorders should involve consideration of a patient's history, including family history of substance use and mental health disorders, as well as the sequence and timelines of the development of symptoms to accurately identify the pre-existing disorder(s).<sup>628-630</sup>

As reviewed in [Ongoing Care—Pharmacotherapy](#), clinicians should consider the potential benefits and risks of prescribing medications for concurrent disorders for each patient and are encouraged to consult or refer to a specialist, where appropriate. Mental health symptoms should be regularly reassessed during initial stages of treatment, as research has shown that AUD treatment can lead to a significant reduction in alcohol-related depression and anxiety symptoms after 2–4 weeks.<sup>836-838</sup> Persistent mental health symptoms would warrant further investigation and treatment that includes evidence-based interventions for both AUD and the mental health condition. Clinicians should also be aware of and accommodate any potential cognitive and functional impairments related to diagnosis of a concurrent mental health disorder.<sup>630</sup>

Depending on the complexity and severity of physical health, mental health, and alcohol-related symptoms, patients with concurrent alcohol and mental health disorders may benefit from a higher intensity or more structured approach to care, such as referrals to inpatient withdrawal management, inpatient treatment programs, or intensive outpatient programs, or to specialist-led psychosocial, addiction medicine, or psychiatric treatment interventions in the community.<sup>734,736,738,741,747</sup> The integration of peer-based support and outreach services (staffed by individuals who have lived experience with concurrent alcohol and mental health disorders, treatment, and recovery) within primary care clinics or referral to such services in the community may also be beneficial for this population.<sup>839-841</sup>

## 8.8 Co-occurring Substance Use Disorders

Individuals with AUD and one or more co-occurring substance use disorders report higher levels of alcohol consumption (i.e., number of drinking days per week, amount of alcohol consumed per drinking day), and exceed low-risk drinking limits more often than individuals with AUD alone.<sup>658</sup>

Reported prevalence rates for co-occurring AUD and other substance use disorders vary in the literature, depending on the source and population studied. Nationally representative US studies have reported that between 15% and 25% individuals with AUD also met diagnostic criteria for another substance use disorder (tobacco, opioids, cocaine, and other unregulated drug[s]) in the past year.<sup>658-660</sup> Conversely, a study of 2,000 treatment-seeking primary care patients found that nearly 75% of those with AUD also met the criteria for one or more co-occurring substance use disorders.<sup>842</sup> Although prevalence rates do vary, it is clear that individuals with co-occurring substance use disorders represent a significant population requiring AUD care.

All individuals with high-risk drinking or AUD should be screened for co-occurring substance use. For those individuals who screen positive, co-occurring substance use disorders should be treated concurrently, when possible, with the severity of each disorder guiding treatment decisions. If concurrent treatment is not possible, patient safety should be prioritized and treatment should be triaged in order of the substance use disorder that carries the highest risk of immediate harm to that individual. Guidance for commonly co-occurring substance use disorders is provided below.

## 8.8.i Co-occurring Alcohol and Smoking/Tobacco Use Disorder

People with AUD or other substance use disorders are more likely to smoke, smoke more heavily, and are less likely to stop smoking than people without AUD or other substance use disorders.<sup>843</sup> Nationally representative U.S. data indicate that between 44% and 51% of individuals who met criteria for an AUD in the past year were also current smokers.<sup>844,845</sup>

Current smoking is associated with increased alcohol consumption, days per month of alcohol consumption, severity of AUD, and severity of alcohol withdrawal symptoms in individuals with AUD.<sup>846,847</sup> In addition, individuals with AUD who use tobacco are more likely to experience negative health consequences, including cognitive impairment and increased risk of cirrhosis, pancreatitis, cardiovascular disease, and some cancers including head and neck cancers.<sup>848-851</sup> Finally, a number of studies have reported that continued smoking is associated with a greater likelihood of relapse to AUD, while tobacco cessation is associated with improved outcomes for individuals engaged in AUD treatment.<sup>852-855</sup>

For the reasons cited above, concurrent or successive tobacco cessation treatment should be prioritized in individuals with AUD who use tobacco<sup>856</sup>; however, a commitment to cessation should not be a requirement for AUD treatment. Although commonly undertreated in substance use treatment programs,<sup>857,858</sup> research has found that between 44–80% of individuals who use tobacco and are seeking treatment for a substance use disorder report an interest in tobacco cessation interventions and motivation to quit smoking.<sup>852,859,860</sup> Further, the addition of tobacco cessation interventions does not appear to negatively impact alcohol- or other substance use-related treatment outcomes in individuals with substance use disorders,<sup>856</sup> and, in some cases, has been associated with improvements. A 2016 Cochrane review (N = 35, n = 5,796) found a consistent association between tobacco cessation interventions—both pharmacotherapy alone and pharmacotherapy combined with counselling—and tobacco abstinence, with no evidence of negative effects on abstinence from alcohol and other substances.<sup>861</sup> Research is also underway to evaluate several combined alcohol and tobacco use disorder interventions in primary care.<sup>862,863</sup>

First-line pharmacotherapies for tobacco cessation—bupropion and varenicline—can be safely prescribed in combination with first-line AUD pharmacotherapies. A 2015 narrative review identified combination therapy with varenicline and naltrexone as the most effective option for reducing both alcohol and tobacco use in individuals with co-occurrence of these substance use disorders.<sup>864</sup>

### 8.8.i.1 Varenicline

Varenicline is a Health Canada-approved medication indicated for smoking-cessation treatment in adults, in conjunction with smoking-cessation counselling.<sup>865</sup> While varenicline has demonstrated effectiveness in reducing smoking, studies examining the effects of varenicline on alcohol consumption have yielded mixed results.<sup>866</sup> Findings from meta-analyses indicate varenicline may reduce alcohol consumption among people with AUD who concurrently smoke cigarettes; however, null effects were reported in terms of heavy drinking days, number of drinks per day, and days abstinent.<sup>866,867</sup> Results from RCTs suggest varenicline may be more effective for some populations, such as men, who had significantly higher rates of no drinking days<sup>868</sup>; older individuals (aged 45 years and above), who had significantly fewer drinking days; people who have been drinking regularly for longer periods of time (i.e., greater than 28 years); and those with a treatment goal of reduced alcohol consumption.<sup>869</sup> Additionally, heavy drinking days, drinks per day, and drinks per drinking day are significantly lower for smokers who also reduced cigarette consumption.<sup>869</sup> Counselling, both substance-specific and integrated (i.e., addressing both nicotine and alcohol use) may be beneficial for some individuals.<sup>870</sup>

Clinicians prescribing varenicline should be aware that some patients who consume alcohol while taking varenicline report increased intoxicating effects, aggressive behaviour, and amnesia.<sup>865</sup> Patients should be advised that alcohol consumption while taking varenicline may increase the risk of experiencing psychiatric adverse events (e.g., suicide ideation and behaviour),<sup>865</sup> although varenicline no longer carries a “black box warning” for serious neuropsychiatric events.<sup>871</sup>



## 8.8.ii Co-occurring Alcohol and Opioid Use Disorder

Co-occurring use of opioids and alcohol is associated with an increased risk of respiratory depression, overdose, and death.<sup>872,873</sup> Approximately one-third of individuals prescribed opioid agonist treatment (OAT) for the management of opioid use disorder (OUD) also meet the criteria for high-risk drinking or AUD.<sup>874-877</sup> Although alcohol use is a known risk factor for fatal overdose among individuals prescribed opioids,<sup>878-880</sup> and individuals who consume alcohol at high-risk levels may experience increased difficulty with adherence to OAT,<sup>881,882</sup> there is limited guidance on effective management strategies for this patient population.<sup>883</sup> One European guideline exists for addressing high-risk alcohol use among people who use drugs, including individuals with OUD, in primary care settings<sup>884</sup> and the [BC Centre on Substance Use](#) (BCCSU) has published an overview of screening and treatment options for individuals with co-occurring AUD and OUD.

Clinicians should screen patients for alcohol or opioid use through validated methods that are familiar and appropriate to their practice, and are not punitive or stigmatizing to patients. A positive result on any screening tool should prompt further assessment to confirm or rule out AUD or OUD based on the DSM-5-TR diagnostic criteria for substance use disorders.

For individuals on OAT who meet criteria for high-risk drinking but do not have AUD, physician or nurse-delivered brief intervention has been found to reduce alcohol consumption in RCTs<sup>885,886</sup> and non-randomized studies.<sup>887-889</sup> Motivational interviewing may also be effective for reducing high-risk drinking in patients prescribed OAT.<sup>890,891</sup> Though not specific to individuals on OAT, the lack of high-quality research in this area was noted in a 2018 meta-analysis of psychosocial interventions to reduce alcohol consumption among people who use illicit drugs (primarily opioids and stimulants).<sup>892</sup> Due to methodological differences between studies (7 RCTs, n = 825), the review authors could only perform a limited number of aggregate analyses, and as a result, no clear recommendations could be made for or against the use of psychosocial interventions for co-occurring high-risk use of alcohol and other substances.<sup>892</sup>

For patients diagnosed with co-occurring AUD and OUD, AUD pharmacotherapy should be offered with consideration of drug–drug interactions with OAT, as

**Acamprosate is the preferred first-line medication for treating those with alcohol and opioid use disorders. Buprenorphine/naloxone may be the preferred option for opioid agonist treatment in this population.**

applicable. More specifically, naltrexone is an opioid antagonist and is contraindicated due to the risk of precipitated withdrawal in patients prescribed opioids, including OAT, or who use unregulated opioids. Thus, acamprosate should be considered as first-line for treating co-occurring AUD in this patient population.<sup>493</sup> Buprenorphine/naloxone, which is a partial opioid agonist, may also be a preferred first-line OAT medication in this patient population due to its superior

safety profile compared to methadone (e.g., lower risk of respiratory depression and overdose, alone or in combination with alcohol),<sup>893</sup> and preliminary evidence showing that high-dose (32mg/day) buprenorphine reduced both alcohol use and craving compared to low-dose buprenorphine and compared to methadone in individuals with co-occurring alcohol and opioid use disorders.<sup>894</sup> Full opioid agonists (e.g., methadone and slow-release oral morphine) should be prescribed with caution and involve close follow-up, as their effect on alcohol use outcomes has not been studied and there is a risk of respiratory depression and drug toxicity when combined with alcohol.

Although gabapentin has a growing evidence base supporting its use for withdrawal management and relapse prevention for AUD,<sup>537</sup> there are specific concerns for individuals with OUD. This includes the possibility of high doses of gabapentin contributing to respiratory suppression, which can increase risk of overdose.<sup>558</sup> If gabapentin is co-prescribed with full opioid agonists, clinicians should be aware of these risks and monitor patients appropriately. Topiramate may be considered for the treatment of AUD in patients who are also on OAT in cases where acamprosate is not appropriate. Topiramate has not been well-studied specifically in this population; however, the efficacy of this medication for the management of AUD is supported by an established body of evidence,<sup>246,608</sup> and it is not contraindicated for patients who use CNS depressants concurrently.<sup>625</sup>

For patients with co-occurring severe OUD and AUD, referral to bed-based treatment facilities may be considered for stabilization to ensure sufficient monitoring and support (e.g., during withdrawal management for AUD or OAT initiation for OUD). Patients may also be connected to peer-based support and outreach services (staffed by individuals who have lived experience with co-occurring substance use disorders, treatment, and recovery) that are based within primary care clinics or in the community.

### 8.8.iii Co-occurring Alcohol and Benzodiazepine Use Disorder

Co-occurring use of benzodiazepine receptor agonists (BZRAs; i.e., benzodiazepines and “z-drugs”) and alcohol is associated with increased risk of respiratory depression, overdose, and death.<sup>895-897</sup> Although Canadian data is lacking, European and U.S. data indicate that 19–41% of individuals seeking or receiving treatment for AUD also report non-medical BZRA use, including DSM-5-TR sedative, hypnotic, or anxiolytic use disorder (hereafter referred to as “sedative use disorder”).<sup>898-901</sup>

There is a lack of evidence-based clinical guidance for the management of co-occurring AUD and sedative use disorder. In the absence of a clear approach and in the context of known risks and harms of combining BZRAs and alcohol, it is recommended that each substance use disorder be treated individually and concurrently. For sedative use disorder, providing patients with evidence-based information on the benefits and risks of BZRA use, alone and in combination with alcohol, can significantly improve patients’ chances of successfully reducing or discontinuing their use.<sup>902</sup> A gradual and stepped dose reduction or taper should be initiated for individuals who have been using BZRAs for more than 4 weeks (whether prescribed or non-medically) and those who meet criteria for a sedative use disorder.<sup>903</sup> In the majority of cases, a BZRA taper can be initiated and monitored safely and effectively in an outpatient primary care setting.<sup>903</sup> Additional guidance on tapering BZRAs in primary care is available from the [College of Family Physicians of Canada](#).<sup>904</sup>

## 8.9 Individuals Experiencing Homelessness

Housing is an important determinant of health that has been linked to a variety of poor health outcomes. Research indicates that living situations such as homelessness and marginal housing (e.g., single-room occupancy housing) are associated with a higher prevalence of chronic and infectious diseases and poorer overall mental and physical health.<sup>905,906</sup> Estimates of substance use among individuals experiencing homelessness vary depending on the population and definition of homelessness used, but there is consistent evidence that individuals experiencing homelessness report disproportionate rates of substance use.

A 2008 meta-analysis of international studies from 1979 to 2005 found that 8.5–58.1% of individuals experiencing homelessness had AUD, with higher prevalence rates found in more recent decades.<sup>907</sup> This is substantially higher than the estimated prevalence rate of 18% in the general population in Canada in 2012, for example.<sup>9</sup> Furthermore, compared to the general population, individuals who experience homelessness have higher alcohol-related consequences and substance-related mortality rates.<sup>908-912</sup>

Current evidence suggests substance use and homelessness are mutually-reinforcing, but evidence is mixed regarding causality, including the direction and magnitude of the relationship between substance use and homelessness.<sup>913</sup> However, housing instability that precedes substance use is linked to increased substance use intensity, with prevalence rates up to 8 times greater than the domiciled population.<sup>24,907,914</sup>

People who use substances and experience homelessness face significant barriers to obtaining or retaining housing because access to housing services has typically been contingent on abstinence from substance use.<sup>913,915,916</sup> In turn, prolonged homelessness and poverty have been shown to exacerbate alcohol use and alcohol-related harms, such as alcohol poisoning, liver disease, poor mental health, social marginalization, injuries from accidents and assaults, and periodic hospitalization and incarceration.<sup>915-917</sup> Additionally, lack of housing stability and unpredictable access to alcohol may result in risky and fluctuating drinking patterns that expose individuals to severe and potentially life-threatening alcohol withdrawal symptoms (e.g., seizures and delirium tremens, death) if alcohol becomes unaffordable or inaccessible.<sup>918</sup> Clinicians should be mindful of the risks associated with non-beverage alcohol use in this population. Non-beverage alcohol use refers to the use of products containing alcohol that are not intended for human ingestion (e.g., mouthwash, hand sanitizer, rubbing alcohol, aftershave, hair spray).<sup>919,920</sup> A study of 150 individuals experiencing homelessness in Edmonton, Alberta found that almost all (88%) reported using alcohol in the previous 6 months, with 1 in 4 individuals reporting consuming non-beverage alcohol.<sup>921</sup> Non-beverage alcohol use is an urgent public health concern among individuals with AUD who experience poverty and homelessness, as it is associated with increased risk of morbidity and mortality due to high alcohol content and harmful additives.<sup>922</sup>

Significant barriers to accessing health care services, including lack of knowledge regarding care options, structural barriers including lack of transportation or lack of child care, not perceiving a need to seek help, and previous and anticipated experiences of discrimination in health care settings may also be present.<sup>921,923</sup> Many people report having multiple unsuccessful experiences with abstinence-based AUD treatment and find goals of discontinuing or reducing alcohol use unrealistic.<sup>915,924</sup> Clinicians can better support individuals who experience homelessness by working collaboratively with patients and their families, when applicable, to determine a harm reduction approach that is low-barrier, low-intensity, non-abstinence focused, and patient-driven, to improve outcomes.<sup>925,926</sup>

**A multidisciplinary team including social work, psychosocial interventions and supports, and addiction care along with community services can be particularly beneficial for people experiencing homelessness.**

Retention in substance use disorder care for individuals experiencing homelessness is low, despite utilizing health care services—particularly emergency services—more frequently than housed individuals.<sup>923</sup> The increased rate of health care utilization may serve as opportunities for clinicians to connect patients with resources to meet their other health, social, and survival needs (e.g., specialist care, housing, food/nutrition/

financial assistance, employment) as requested or appropriate. Research has shown that access to a multidisciplinary approach managed by a team with expertise in addiction medicine, social work, and psychology in a supportive community led to a decrease in alcohol consumption and an improvement in overall living and working conditions for individuals experiencing homelessness.<sup>911</sup>

## 8.10 Rural and Remote Populations

As of 2021, approximately 6.6 million Canadians live in a rural area, with a 0.4% population increase from 2016.<sup>927</sup> Notably, 14% of Indigenous people in Canada live in rural areas and another 40% live on-reserve.<sup>753</sup> Canadians living in rural areas were more likely to report heavy drinking (22.4%), compared to their counterparts residing in urban areas (18.4%).<sup>928</sup>

There are unique barriers to both accessing and providing substance use disorder care in rural and remote areas. The most commonly reported barrier to substance use care is the lack of treatment services, followed by increased travel times.<sup>929</sup> Rural and remote communities are less likely to have clinics or pharmacies in their communities, necessitating travel to other communities to access substance use disorder care, which can be costly and time-consuming for patients. Moreover, individuals who live in rural and remote communities are more likely to be undiagnosed and untreated for substance use disorders and more likely to report unmet substance use care needs.<sup>930-932</sup> At the provider level, health care providers in rural and remote areas are also less likely to have received training in either specialized addiction care or AUD medications and, as a result, are less likely to offer their patients evidence-based treatments.<sup>932</sup> However, not all rural communities are alike, and it is crucial to ensure health care services are tailored toward the community's unique needs.

### 8.10.i Virtual Care

One strategy to mitigate barriers to engagement and retention in care is the use of virtual care, which enables prescribers and specialists to consult with patients from a distance. Virtual care may be used along with in-person appointments to reduce travel time for patients and facilitate referrals without onerous travel. The use of virtual care has been shown to improve access to care and reduce heavy drinking when combined with treatment as usual, particularly in rural populations.<sup>933,934</sup> Virtual care can also provide clinical flexibility in other scenarios such as local or global emergencies (see [Clinical Flexibility in Response to Local or Global Events and Reducing Barriers](#)). Virtual care treatment for substance use disorder care may help engage patients in their care by improving access and convenience and was shown to be at least as effective as in-person treatment in terms of retention, therapeutic alliance, and substance use during the COVID-19 pandemic.<sup>935</sup>

Poverty and access to technology may pose barriers to virtual care, as not all individuals have access to a telephone or internet services. Cited barriers to using virtual care include lack of high-speed internet access, which disproportionately affects racial minorities, older adults, and those with low levels of education.<sup>936</sup> Clinical judgment and patient circumstances should guide when and if virtual care

is appropriate. Examples of situations in which virtual care may be considered to reduce patient burden include:

- Follow up and ongoing care
- Providing support for patients undergoing outpatient withdrawal management
- Patient assessment following a new pharmacotherapy

In addition to using clinical judgment, prescribers must adhere to relevant practice standards in their jurisdiction regarding virtual care. Prior to providing virtual care, patient consent must be obtained and documented, and the clinician must describe the limitations of virtual care (e.g., limited physical exam, limits in sound and image, potential for security breaches).

# 9 Managed Alcohol Programs

Managed alcohol programs (MAPs) are a harm reduction intervention that aim to minimize the adverse personal and societal effects of severe AUD, particularly as experienced by individuals who may be experiencing homelessness or who are unstably housed.<sup>307,308</sup> Managed alcohol provision typically involves dispensing individually-tailored doses of alcohol to clients at regular intervals to regulate alcohol intake, minimize the risk of developing severe alcohol withdrawal symptoms due to lack of access to alcohol, and reduce or eliminate the need for consuming non-beverage alcohol (e.g., hand sanitizer, mouthwash, rubbing alcohol, hair spray).<sup>307</sup>

In Canada, MAPs operate in hospital- or community-based settings. In the community, MAPs are often coupled with, or offered within, housing programs to provide a safe and inclusive alternative to abstinence-only housing for individuals with severe AUD.<sup>308</sup> This low-threshold approach<sup>ba</sup> enables clients to gain access to other health and social services that may be offered within the program.<sup>307</sup> In acute care settings, MAPs have also been implemented to support patients with severe AUD for whom withdrawal management or short-term abstinence during their hospital stay is not feasible.<sup>937</sup> For a list of MAP services across Canada, refer to the Canadian Institute for Substance Use Research's [Overview of MAP Sites in Canada](#).

Several controlled studies of community-based MAPs have reported evidence of significant benefit on a number of key outcomes of interest including reduced alcohol-related harms, reduced use of non-beverage alcohol, improved quality of life and safety, improved housing stability, and reduced burden on the health and criminal justice systems.<sup>938-943</sup> For example, a 2018 observational study compared alcohol consumption of participants (n = 175) from six bed-based MAPs across Canada (two in Ottawa, and one each in Vancouver, Thunder Bay, Toronto, and Hamilton) with a control group matched for age, sex, and ethnicity (n = 189).<sup>944</sup> Results showed that participants who had been MAP clients for longer than two

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ba This document defines low-threshold programs as those with one or more of the following elements: universal cost-coverage, community-based prescribing (where relevant) and dispensation, rapid access, no specified maximum dose or treatment duration, and no strict requirements for abstaining from alcohol use.



months had fewer standard drinks per day (15.1 drinks, 95% CI: 13.34 to 17.09;  $p < .001$ ) than newer MAP participants (20.2 drinks, 95% CI: 17.48 to 23.36) and controls (22.2, 95% CI: 20.36 to 24.25), with a significant difference in drinks per day between older and newer MAP clients ( $p < .01$ ).<sup>944</sup> Long-term MAP residents were also significantly less likely to report a range of alcohol-related harms (e.g., physical health issues, involvement in illegal activities, social problems) over the past 30 days than newer MAP participants and controls.<sup>944</sup>

The long-term (12-month) impact of MAPs on alcohol use trends and related health harms was examined by a 2021 multi-site quasi-experimental longitudinal study involving 59 MAP participants in comparison to 116 local controls who were not receiving treatment for their AUD and would have met MAP entry criteria.<sup>945</sup> While both groups exhibited similarly reduced total consumption of beverage and non-beverage alcohol, MAP participants consumed their alcohol in a more even and measured pattern, with their total alcohol consumption spread out over a longer period of time (25.41 versus 19.64 days per month). Managed alcohol participants also reported significantly fewer harms than controls at both 2- and 6-month follow-up. While affirming the findings of previous MAP studies summarized above, this article provides the most robust evidence to date suggesting that MAP participation can promote a safer and more stable pattern of alcohol consumption compared to controls, with no negative impact on liver function or other alcohol-related health harms.<sup>945</sup>

Additionally, qualitative research findings on community-based MAPs to date suggest that, in addition to mitigating alcohol-related risks and facilitating access to basic health care and nutrition, MAPs offer clients a safe and stable space where they can restore their social and cultural connections and begin to heal.<sup>915,919</sup>

The hospital-based inpatient provision of alcohol to prevent and manage severe alcohol withdrawal is supported by a relatively small body of evidence. A 2018 review of 28 articles (n = 688 participants), including 5 randomized and 1 non-randomized controlled trials, found the provision of alcohol to be safe and non-inferior to standard withdrawal management protocols (e.g., treatment with benzodiazepines) for preventing or treating alcohol withdrawal symptoms among hospitalized patients with severe AUD.<sup>937</sup>

While making explicit recommendations on the use of MAPs as a harm reduction strategy is outside the scope of this guideline, the committee wishes to acknowledge the growing body of evidence supporting this approach for individuals with severe AUD and recognizes MAPs as part of the AUD continuum of care. Further information and suggestions to support the implementation of MAPs in community and clinical care settings as a part of a comprehensive strategy to reduce the significant harms experienced by individuals with severe AUD is available in the [Canadian Operational Guidance for MAPs](#).

# 10 Summary

Despite the significant burden of disease, social harms, and economic costs associated with alcohol use in Canada, high-risk drinking and AUD frequently go unrecognized and untreated in the health care system. Recent literature has highlighted the vital role of primary care providers in meeting the health care needs of individuals with AUD.<sup>72</sup> This guideline contains evidence-based clinical recommendations for the identification, intervention, management, and ongoing care of individuals with high-risk drinking and AUD.

This guideline emphasizes the importance of providing education to patients about *Canada's Guidance on Alcohol and Health* and performing routine screening for alcohol use above lower-risk limits. Research shows that simple validated screening procedures can be incorporated in primary care routines to reliably identify high-risk drinking and AUD, whereas the current reliance on case identification alone often results in missed opportunities for the timely detection of individuals at risk.<sup>28</sup> In many cases, symptoms of excessive alcohol use may be misdiagnosed (e.g., mild alcohol withdrawal diagnosed as anxiety) and treated with costly and ineffective interventions. Additionally, identification of high-risk drinking enables clinicians to intervene at a point where the secondary prevention of AUD is possible through brief interventions.<sup>144,145,246</sup> As such, this guideline recommends routine alcohol use screening of all adult and youth patients, followed by brief intervention in patients who screen positive for high-risk alcohol use. These patients should undergo a diagnostic interview for AUD using DSM-5-TR criteria and further assessment to inform a treatment plan if indicated.

Up to 50% of individuals with long-term AUD will experience alcohol withdrawal symptoms upon cessation or rapid reduction of drinking.<sup>267-269</sup> Research has shown that appropriate clinical management of withdrawal symptoms can prevent the development of a severe alcohol withdrawal syndrome, including seizures and delirium tremens, as well as early relapse.<sup>260,261</sup> To facilitate risk-based withdrawal management planning, this guideline recommends using the Prediction of Alcohol Withdrawal Severity Scale (PAWSS), a score-based, clinician-administered tool for assessing the risk of severe withdrawal, along with clinical parameters such as past delirium tremens and/or seizures.

This guideline recommends outpatient withdrawal management for patients who are at low risk of developing severe withdrawal (e.g., PAWSS < 4) and have no other comorbid conditions that would be a contraindication to outpatient management.<sup>297,298,300</sup> For management of patients at risk of mild to moderate withdrawal who would benefit from pharmacotherapy to manage withdrawal symptoms, this guideline recommends offering non-benzodiazepine medications, such as carbamazepine, gabapentin, and clonidine.<sup>335,338-341</sup> Patients at high risk of developing severe withdrawal (e.g., PAWSS ≥ 4) should be referred to an inpatient setting where alcohol withdrawal can be medically supervised and closely monitored. Benzodiazepines remain the preferred option for the treatment of patients at risk of severe alcohol withdrawal, because only benzodiazepines have demonstrated efficacy for preventing seizures and delirium tremens.<sup>319-321</sup> Ideally, benzodiazepines should be prescribed in an inpatient setting where patients can be closely observed, but may be offered to closely-monitored outpatients, due to the safety concerns with benzodiazepines.<sup>258</sup> This guideline strongly recommends that all patients who complete withdrawal management be offered a connection to ongoing AUD care, treatment, and support. Withdrawal management alone does not constitute treatment for AUD as demonstrated by high post-withdrawal relapse rates reported in the literature.<sup>381-387</sup>

Patients who are diagnosed with AUD should be offered a full range of evidence-based psychosocial and pharmacological treatment interventions. Treatment and support should be individually tailored and adjusted appropriately based on AUD severity, concurrent disorders, psychosocial circumstances, as well as evolving patient preferences and needs. This document reviewed the evidence on the safety and efficacy of a range of psychosocial and pharmacological treatment interventions that can be offered as part of an ongoing care strategy in the clinical management of AUD. This guideline recommends that all patients with AUD receive information about and referrals to specialist-led psychosocial treatment interventions (e.g., cognitive behavioural therapy, family-based therapy) where available, as well as peer-based support groups and other recovery-oriented services in the community. The evidence suggests that psychosocial treatments may have a modest but significant impact on likelihood of relapse and return to heavy drinking among youth and adult patients.<sup>406,407,450-453,460</sup> The committee recognizes the value of peer-based support, guidance, and mentorship to patients and families in navigating changes during the process of recovery and wellness, and recommends that clinicians provide all patients and families affected by AUD

with information on and referrals to local peer support groups (e.g., Alcoholics Anonymous, SMART Recovery, LifeRing Secular Recovery) .<sup>703,704,732</sup>

Evidence-based pharmacotherapies have been shown to play an important role in supporting the achievement of treatment goals among patients with moderate to severe AUD, but they are underutilized in primary care practice. As a part of a comprehensive long-term treatment and support plan, evidence-based pharmacotherapy can help prevent a return to drinking among patients whose goal is abstinence, and reduce heavy drinking episodes and overall alcohol intake for patients who wish to reduce their alcohol consumption.<sup>261</sup> There is a well-established evidence base that supports offering naltrexone or acamprosate as a first-line pharmacotherapy medication to all patients with moderate to severe AUD.<sup>31,261,487,493,946,947</sup> More specifically, naltrexone is recommended for patients with a treatment goal of abstinence or reduced drinking, and acamprosate is recommended for patients with a treatment goal of abstinence.<sup>261,479,516</sup> For patients for whom first-line medications are not appropriate or preferable, this guideline recommends gabapentin or topiramate, which are supported by a growing body of evidence.<sup>523,537,604</sup> This guideline also recommends against prescribing SSRI antidepressants or antipsychotics for the treatment of AUD and SSRI antidepressants for patients with AUD and a concurrent anxiety or depressive disorder, as these interventions have not demonstrated efficacy for alcohol outcomes or mood symptoms. Furthermore, clinicians should not prescribe benzodiazepines as a long-term treatment for AUD outside the context of acute withdrawal management.

While this guideline has presented specific evidence-based recommendations for the optimal screening, diagnosis, treatment, and care of individuals with AUD, the committee recognizes the need for further work to develop an integrated and comprehensive system of substance use care in each jurisdiction in Canada, including a robust continuum of evidence-based care options that are available and accessible to all patients and families across the country. Additionally, the committee recognizes the need to enhance collaboration between different sectors and across the continuum of care to better support patients and families as they navigate the treatment and recovery process. The present document is intended to serve as a foundation for the development of policies, practice tools, and educational resources that will enable primary care clinicians to assume a central role within this emerging system of care.

# Appendices

## Preface

The following appendices have been provided to support clinical practice and were developed using a different methodology than the main guideline. Here, guidance has been adapted from the appendices contained in the BC provincial AUD guideline, which were derived through discussion and consensus of an interdisciplinary working group convened in addition to the guideline committee. The Canadian Alcohol Use Disorder Guideline's committee provided further feedback based on their expertise on these appendices. The practice guidance herein was informed by review of existing national and international evidence-based clinical practice guidelines issued by recognized addiction medicine organizations and authorities. Where appropriate, Health Canada-approved drug product monographs were consulted to ensure compliance with provincial and national safety regulations and standards for practice.

# Appendix 1: Methods

## A1.1 Funding

Guideline development activities were supported by grant funding from Health Canada's Substance Use and Addictions Program. The Canadian Research Initiative in Substance Misuse supported the guideline's co-chairs (Drs. Wood and Rehm) and the British Columbia Centre on Substance Use provided in-kind support. This guideline was developed without support from the pharmaceutical industry or associated stakeholders.

## A1.2 Committee Membership

An interdisciplinary committee of 36 individuals was assembled in December 2020, including representation from across Canada, with expertise spanning addiction medicine, psychiatry, family practice, social work, nursing, pharmacy, recovery-oriented systems of care, health care administration and policy, and people and family members with lived and living experience of alcohol use. Notably, several committee members with lived experience had lost contact with the committee during the project and were unreachable at the final stages of approval. Their meaningful contributions are included in this work.

### A1.2.i Conflict of Interest Policy

In keeping with Guidelines International Network's Principles for Disclosure of Interests and Management of Conflicts,<sup>948</sup> committee members were required to disclose all sources and amounts of direct and indirect remuneration received in the past five years from industry, for-profit enterprises, and other entities (i.e., direct financial conflicts) that could introduce real, potential, or perceived risk

of bias. In addition, committee members were asked to report possible indirect conflicts of interest, such as academic advancement, clinical/professional revenue, and public standing that could potentially influence interpretation of evidence and formulation of the strategies contained in this guidance. Disclosures were collected from all committee members in 2020 and 2023.

## **A1.2.ii Conflict of Interest Summary**

No committee members disclosed direct monetary or non-monetary support from industry sources within the past five years. One committee member disclosed potential direct conflict of interests involving current employment at a mixed private-/public-pay addiction treatment facility. No committee members disclosed direct financial conflicts in the form of paid consulting or advisory board participation, or paid honoraria for lectures/training. One committee member disclosed receiving monetary support from D&A Pharma for review activities (i.e., data monitoring boards, statistical analysis, and endpoint committees for relevant technology or intervention [n = 1; total value 3,075 Euros; year 2016]).

In terms of indirect sources of potential interest or bias, overall, 16 of 36 individuals disclosed special interests in relation to the content of this document. These pertained to expertise or clinical practice (e.g., addiction medicine clinician, clinic staff, academic addictions expert), advisory board or committee membership, expert testimony, public statements, or past or current research activities on treatment interventions or approaches reviewed in this document. None of the research activities were related to primary studies of AUD treatment efficacy and none were industry-funded. No committee members reported that their clinical revenue could potentially be influenced by the guidance in this document.

Upon review, of those who disclosed potential direct or indirect conflicts of interest or bias, none were deemed to be of sufficient relevance or weight to warrant exclusion from the committee. To mitigate any real, potential, or perceived risk of bias, the committee member who disclosed a direct potential conflict of interest involving employment with an addiction treatment facility was recused from voting on any recommendations pertaining to community-based supports and recovery.



## A1.3 Guideline Development Process

Consistent with best practices for guideline development, the AGREE-II instrument<sup>949</sup> was used throughout development and revision phases to ensure the guideline met international standards for transparency, high quality, and methodological rigour. Guideline development followed the ADAPTE process—a structured approach to adapting an existing guideline for a new context.<sup>950</sup> For this work, the British Columbia Provincial Guideline for the Clinical Management of High-Risk Drinking and Alcohol Use Disorder<sup>951</sup> was adapted for a Canada-wide audience.

Between December 2020 and December 2022, the guideline committee conferred through email and virtual meetings. At the first committee meeting, the outline, scope, and topics of the guideline were provisionally approved by committee consensus.

Three working groups were struck and assigned core sections of the guideline: (1) Screening, Diagnosis, and Brief Intervention, (2) Withdrawal Management, and (3) Ongoing Care. Between December 2020 and December 2022, each working group conferred over email and video conference to discuss and approve draft guideline contents and recommendations. During this process, the working groups were given brief evidence summaries for each clinical question followed by draft text of each chapter. The working groups reviewed the materials and provided feedback, which was incorporated into the next draft. The cycle of review and revision occurred several times, until the working groups achieved consensus on the text and recommendations.

### A1.3.i Development and Approval of Recommendations

Each working group determined through consensus whether the drafted recommendations in their respective sections should be accepted without modification, adapted, or removed. The majority of the recommendations were originally developed for the BC Provincial Guideline. The working groups used the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) tool<sup>1</sup> to score all recommendations.

### A1.3.i.1 GRADE Quality of Evidence

Initial estimates of quality are based on a traditional hierarchy of evidence, whereby meta-analyses of randomized clinical trials are assigned the highest score, followed by individual clinical trials, quasi- or non-randomized trials, observational studies and reports, and expert opinion, which is assigned the lowest score. Factors that lowered confidence in the estimated effect of an intervention included risk of bias, inconsistency across the RCTs, indirectness, and publication bias; factors that increased confidence include large effect sizes and an observed dose-response effect. The final quality ratings are reflective of the estimated effect of an intervention as reported in the literature with consideration of biases and limitations of the evidence base as identified by the committee.

Table 3. GRADE Quality of Evidence

Quality of Evidence	Definition
High	Further research is very unlikely to change our confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low	Any estimate of effect is very uncertain

### A1.3.i.2 GRADE Strength of Recommendation

To determine strength of recommendations, the GRADE system takes into account the quality of evidence as well as additional factors, such as clinician, patient, and policy maker's values and preferences, costs and cost-effectiveness, risk-benefit ratios, and feasibility.<sup>952</sup>

Table 4. GRADE Strength of Recommendation

Strength of Recommendation	Definition
Strong	Implies that all patients in the given situation would want the recommended course of action and that only a small proportion of patients would not
Conditional	Implies that most patients in the given situation would want the recommended course of action but many would not

Once approved by the respective working groups, the full-text draft guideline and graded recommendations were compiled and circulated to the full committee. The committee was given three weeks to submit written feedback on the draft guideline. A committee meeting was held in December 2022 to review and discuss the feedback. Feedback was collated and incorporated into a revised draft for external review.

### A1.3.ii External Review

The draft guideline was circulated for review and comment to 13 relevant experts and stakeholders from Canada and international jurisdictions as identified by the committee. Expertise included addiction medicine, psychiatry, psychology, evidence-based medicine, and Indigenous health. All external reviewers completed conflicts of interest disclosure forms prior to review in January 2023. Feedback from the external reviewers was reviewed by the co-chairs and incorporated into the guideline.

The revised version text was distributed to the guideline committee. Of the 36 members, 35 provided their approval of the final version of the guideline in May 2023.

### A1.3.iii Update Schedule

The guideline will be regularly reviewed to determine ongoing relevance and whether updates are required.

## A1.4 Literature Search Strategy

### A1.4.i General overview

The national guideline expanded on the systematic literature search conducted for the [Provincial Guideline for the Clinical Management of High-Risk Drinking and Alcohol Use Disorder](#), developed in British Columbia by the BC Centre on Substance Use, Ministry of Health, and Ministry of Mental Health and Addictions and published in December 2019. For the BC provincial guideline, a systematic literature search was conducted in 2018.

For this national guideline, an information specialist performed the literature searches using a peer-reviewed search strategy for the following databases: Medline, Embase, Cochrane Database of Systematic Reviews, and Cochrane Central Register of Controlled Trials via Ovid; and CINAHL and PsycINFO via EbscoHost. Where subjects are well-indexed, subject headings were used to increase relevance and precision of search results and to ensure a manageable number of items retrieved; where subjects are less well-indexed, or had not yet been assigned subject headings, key words were added to increase recall. Subject headings used were database dependent, but analogous to the Medical Subject Headings (MeSH) used in Medline. Search fields were expanded to include author-assigned keywords, an approach that was not utilized in the initial 2018 literature search. Search date limits varied by topic; for topics with a high-quality systematic review or meta-analysis, the search began in the year of publication for the most recent review. Studies were excluded if they did not meet inclusion criteria established *a priori* or if they were already included in high-quality systematic reviews and meta-analyses. There was no search of unpublished research. Additional details of the search strategies are provided below and a full list of search terms can be found at: <https://www.bccsu.ca/alcohol-use-disorder/canadian>. Following the completion of the literature searches, additional articles were further identified through targeted searching and from references lists in selected articles.

Two medical writers independently screened and identified eligible studies. Discordance between reviewers on inclusion or exclusion of individual studies was resolved through discussion with no need for arbitration. The [PRISMA](#) flowcharts

are included below. One reviewer used validated assessment tools (e.g., AMSTAR-2, Cochrane Risk of Bias Tool, Downs and Black checklist) to evaluate study quality.

#### **A1.4.ii September 2020 Literature Search**

The committee co-chairs reviewed the 2018 strategy and approved of search terms and parameters along with additional keywords related to the single question alcohol screen, the NIAAA screening tool, contingency management, Vivitrol, and Depade. The updated search was conducted on September 24 and 25, 2020.

##### **The interventions and publication dates addressed in this search were:**

1. Screening tools (2013–2020)
2. Brief intervention (2011–2020)
3. Withdrawal symptoms risk/severity assessment tools (2013–2020)
4. Withdrawal Management pharmacotherapies (2010–2020)
5. Ongoing Care
  - a. Pharmacotherapies (2014–2020)
  - b. Psychosocial treatments, including recovery support services and psychosocial supports (2005–2020)

Table 5. Inclusion and Exclusion Criteria for September 2020 Literature Search

Research Question	Include	Exclude
<b>Screening, Diagnosis and Brief Intervention</b>		
1. What screening tools are available and how do different screening tools compare to one another for detection of high-risk drinking or AUD in clinical care settings?	<ul style="list-style-type: none"> <li>• 1–2 question screening, CAGE, TWEAK, AUDIT, CRAFFT, NIAAA</li> <li>• Population: Adults, adolescents and young adults (12–25), older adults, with AUD, high-risk drinking, binge drinking, or other drinking exceeding limits of Canadian LRDG</li> <li>• Study types: Systematic reviews, meta-analyses, clinical trials, quasi-experimental studies, guidelines</li> <li>• Language: English</li> <li>• Year: 2013–forward</li> </ul>	<ul style="list-style-type: none"> <li>• Incarcerated populations</li> <li>• Screening for other substance use disorders</li> <li>• Non-English language publications</li> <li>• Opinion, letter to the editor, narrative review</li> </ul>
2. What is the evidence that screening followed by brief behavioural counselling intervention (with or without referral to treatment) is effective for reducing harms associated with high-risk drinking or AUD?	<ul style="list-style-type: none"> <li>• Related to alcohol use disorder, high-risk drinking, or alcohol-related harms</li> <li>• Screening</li> <li>• Brief intervention</li> <li>• Population: Adults, adolescents and young adults (12–25), older adults, with AUD, high-risk drinking, binge drinking, or other drinking exceeding limits of Canadian LRDG</li> <li>• Study types: Systematic reviews, meta-analyses, clinical trials, quasi-experimental studies, guidelines</li> <li>• Language: English</li> <li>• Year: 2011–forward</li> </ul>	<ul style="list-style-type: none"> <li>• Incarcerated populations</li> <li>• Screening or brief intervention for other substance use disorders</li> <li>• Non-English language publications</li> <li>• Opinion, letter to the editor, narrative review</li> </ul>
<b>Risk Assessment and Withdrawal Management</b>		
1. What evidence-based approaches are available for predicting the severity of alcohol withdrawal in order to select the optimal treatment pathway?	<ul style="list-style-type: none"> <li>• PAWSS</li> <li>• Luebeck Alcohol Withdrawal Scale</li> <li>• CIWA</li> <li>• Population: Adults, adolescents and young adults (12–25), older adults, with AUD, high-risk drinking, binge drinking, or other drinking exceeding limits of Canadian LRDG</li> <li>• Study types: Systematic reviews, meta-analyses, clinical trials, quasi-experimental studies, guidelines</li> <li>• Language: English</li> <li>• Year: 2013–forward</li> </ul>	<ul style="list-style-type: none"> <li>• Incarcerated populations</li> <li>• Non-English language publications</li> <li>• Opinion, letter to the editor, narrative review</li> </ul>
2. 2. What pharmacotherapies are effective for managing alcohol withdrawal?	<ul style="list-style-type: none"> <li>• Benzodiazepines</li> <li>• Anticonvulsants (gabapentin, valproic acid, carbamazepine)</li> <li>• Alpha-2 adrenergic agonists (clonidine)</li> <li>• Non-pharmacological approaches</li> <li>• Supportive therapy (e.g., electrolytes, vitamin supplementation, OTC medications)</li> <li>• Population: Adults, adolescents and young adults (12–25), older adults, with AUD, high-risk drinking, binge drinking, or other drinking exceeding limits of Canadian LRDG</li> <li>• Study types: Systematic reviews, meta-analyses, clinical trials, quasi-experimental studies, guidelines</li> <li>• Language: English</li> <li>• Year: 2010–forward</li> </ul>	<ul style="list-style-type: none"> <li>• Incarcerated populations</li> <li>• Studies on above medications not relevant to alcohol withdrawal</li> <li>• Non-English language publications</li> <li>• Opinion, letter to the editor, narrative review</li> </ul>

## Ongoing Care

<p>1. What pharmacotherapies are effective for the treatment of AUD?</p>	<ul style="list-style-type: none"> <li>• Naltrexone</li> <li>• Acamprosate</li> <li>• Disulfiram</li> <li>• Gabapentin</li> <li>• Topiramate</li> <li>• Baclofen</li> <li>• Ondansetron</li> <li>• Varenicline</li> <li>• Combination pharmacotherapies</li> <li>• Population: Adults, adolescents and young adults (12–25), older adults, with AUD, high-risk drinking, binge drinking, or other drinking exceeding limits of Canadian LRDG</li> <li>• Study types: Systematic reviews, meta-analyses, clinical trials, quasi-experimental studies, guidelines</li> <li>• Language: English</li> <li>• Year: 2014–forward</li> </ul>	<ul style="list-style-type: none"> <li>• Incarcerated populations</li> <li>• Studies on above medications not relevant to alcohol use disorder</li> <li>• Non-English language publications</li> <li>• Opinion, letter to the editor, narrative review</li> </ul>
<p>2. What psychosocial treatment interventions and recovery supports are effective for the treatment of AUD?</p>	<ul style="list-style-type: none"> <li>• Motivational interviewing and motivational enhancement therapy</li> <li>• Cognitive behavioural therapy</li> <li>• Contingency management</li> <li>• Family-based therapy (including partner/couples, family network, etc.)</li> <li>• Mindfulness</li> <li>• Dialectical behavioural therapy</li> <li>• Peer-support groups (12-step, Alcoholics Anonymous, SMART, LifeRing, etc.)</li> <li>• Residential/bed-based treatment and therapeutic communities</li> <li>• Supportive recovery housing</li> <li>• Psychosocial supports: housing, vocational programs, legal services</li> <li>• Other psychosocial treatment or support for AUD</li> <li>• Population: Adults, adolescents and young adults (12–25), older adults, with AUD, high-risk drinking, binge drinking, or other drinking exceeding limits of Canadian LRDG</li> <li>• Study types: Systematic reviews, meta-analyses, clinical trials, quasi-experimental studies, guidelines</li> <li>• Language: English</li> <li>• Year: 2005–forward</li> </ul>	<ul style="list-style-type: none"> <li>• Incarcerated populations</li> <li>• Studies on above interventions not relevant to alcohol use disorder</li> <li>• Non-English language publications</li> <li>• Opinion, letter to the editor, narrative review</li> </ul>

<p>3. What combinations of psychosocial and pharmacotherapy treatment interventions are effective for the treatment of AUD?</p>	<ul style="list-style-type: none"> <li>• Pharmacotherapies</li> <li>• Naltrexone</li> <li>• Acamprosate</li> <li>• Disulfiram</li> <li>• Gabapentin</li> <li>• Topiramate</li> <li>• Baclofen</li> <li>• Ondansetron</li> <li>• Varenicline</li> <li>• Combination pharmacotherapies</li> <li>• Psychosocial treatment interventions</li> <li>• Motivational interviewing and motivational enhancement therapy</li> <li>• Cognitive behavioural therapy</li> <li>• Contingency management</li> <li>• Family-based therapy (including partner/couples, family network, etc.)</li> <li>• Mindfulness</li> <li>• Dialectical behavioural therapy</li> <li>• Peer-support groups (12-step, Alcoholics Anonymous, SMART, LifeRing, etc.)</li> <li>• Residential/bed-based treatment and therapeutic communities</li> <li>• Supportive recovery housing</li> <li>• Psychosocial supports: housing, vocational programs, legal services</li> <li>• Other psychosocial treatment or support for AUD</li> <li>• Population: Adults, adolescents and young adults (12–25), older adults, with AUD, high-risk drinking, binge drinking, or other drinking exceeding limits of Canadian LRDG</li> <li>• Study types: Systematic reviews, meta-analyses, clinical trials, quasi-experimental studies, guidelines</li> <li>• Language: English</li> <li>• Year: 2005–forward</li> </ul>	<ul style="list-style-type: none"> <li>• Incarcerated populations</li> <li>• Studies on above interventions not relevant to alcohol use disorder</li> <li>• Non-English language publications</li> <li>• Opinion, letter to the editor, narrative review</li> </ul>
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Records from database searches were downloaded and imported into an EndNote database to facilitate removal of duplicates and article screening.

Limitations:

- Grey literature resources were not searched for this phase of the literature search.
- Unpublished studies and clinical trial registries were not searched.

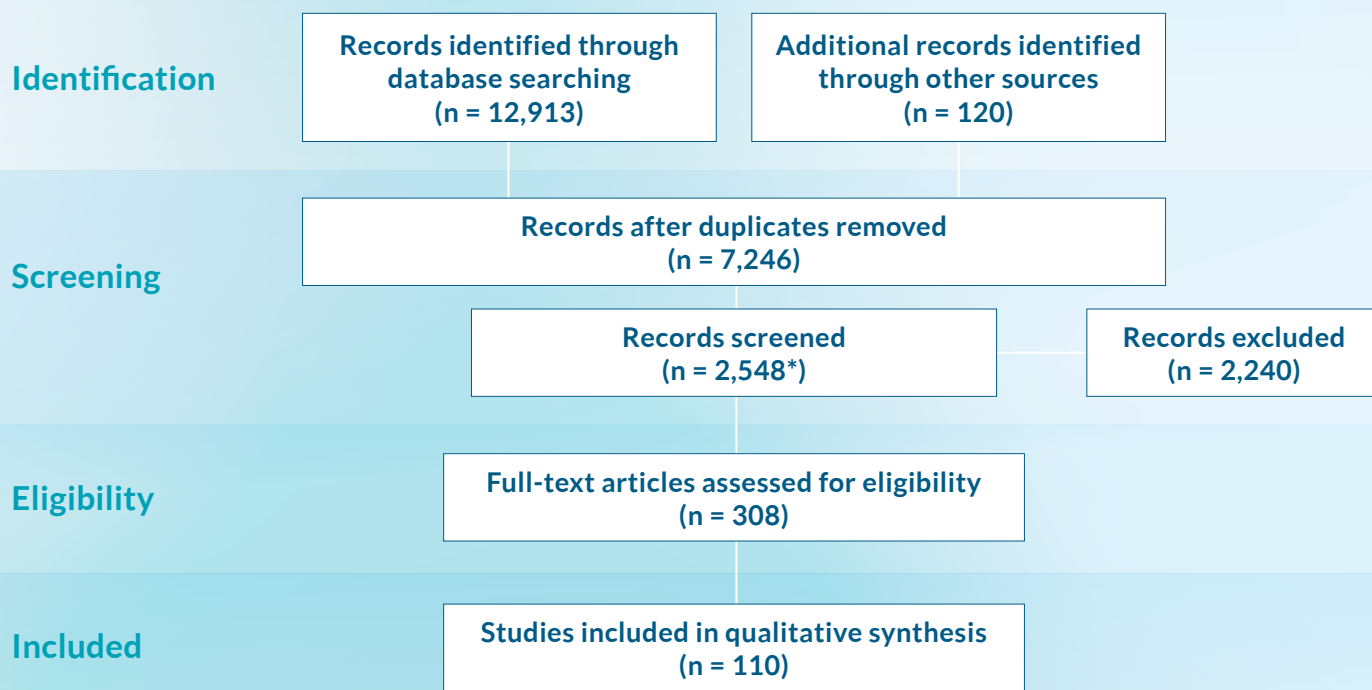


Table 6. Items Identified by Database or Resource Type  
(2020 Update—Includes results of 2018 search)

Database Name	Number of items Identified	Number of items (Duplicates Removed)
Medline	3,411 (3,381 after deduplicating in Ovid)	3,321
CDSR	44	42
EMbase	4,273 (4,055 after deduplicating in Ovid)	1,698
CINAHL	2,931	1,295
PsycINFO	2,254	770
<b>Total – All Sources</b>	12,913 (12,655 after deduplicating in Ovid)	7,126

In total, there were 2,428 records identified in the updated literature search that had not been included in the 2018 search results.

## PRISMA Flow Chart – September 2020 Literature Search



\*Only new records that were not included in the initial 2018 literature search were screened.

### **A1.4.iii May 2022 Literature Search—Prescribing Patterns to Avoid**

Following discussion with the committee and co-chairs, a new literature search strategy was developed and conducted to identify published articles related to the use of antidepressants and antipsychotics as ongoing care medications for AUD and longer-term benzodiazepine prescribing for individuals with AUD (i.e., benzodiazepine prescribing outside of withdrawal management).

A limited but systematic literature search was conducted to identify key published material in English published from 2000 to 2022 addressing the use of antidepressants, antipsychotics, and longer-term benzodiazepines in the context of AUD. Specific search parameters (e.g., inclusion/exclusion criteria, jurisdictions, time frame, languages of publication) were developed by the medical writers and committee co-chairs. The search was conducted on May 12, 2022.

Table 7. Inclusion and Exclusion Criteria for Prescribing Patterns to Avoid Literature Search

Research Question	Include	Exclude
1. Are antidepressants effective in treating AUD?	<ul style="list-style-type: none"> <li>• Intervention: Antidepressants (Selective serotonin reuptake inhibitors (SSRI), Serotonin–norepinephrine reuptake inhibitors (SNRI), Serotonin modulators and stimulators (SMS or serotonin modulator), Serotonin antagonists and reuptake inhibitors (SARI), Norepinephrine reuptake inhibitors (NRI or NERI), Norepinephrine-dopamine reuptake inhibitors OR bupropion)</li> <li>• Comparator: Placebo, alcohol use disorder pharmacotherapies (e.g., naltrexone, acamprosate, gabapentin, topiramate)</li> <li>• Outcome: Alcohol-related outcomes (e.g., quantity or frequency of alcohol use, harms), Mental health outcomes, Psychosocial outcomes</li> <li>• Population: Adults, adolescents and young adults (12–25), older adults, with AUD, high-risk drinking, binge drinking, or other drinking exceeding limits of Canadian LRDG</li> <li>• Study types: Systematic reviews, meta-analyses, clinical trials, quasi-experimental studies, guidelines</li> <li>• Language: English</li> <li>• Year: 2000–forward</li> </ul>	<ul style="list-style-type: none"> <li>• The following category of antidepressants should be excluded: Tricyclic antidepressants, Tetracyclic antidepressants, Monoamine oxidase inhibitors, NMDA receptor agonists</li> <li>• Incarcerated populations</li> <li>• Non-English language publications</li> <li>• Opinion, letter to the editor, narrative review</li> </ul>
2. Are antipsychotics effective in treating AUD?	<ul style="list-style-type: none"> <li>• Intervention: Antipsychotics (typical or first-generation, atypical or second-generation)</li> <li>• Comparator: Placebo, alcohol use disorder pharmacotherapies (e.g., naltrexone, acamprosate, gabapentin, topiramate)</li> <li>• Outcome: Alcohol-related outcomes (e.g., quantity or frequency of alcohol use, harms), Mental health outcomes, Psychosocial outcomes</li> <li>• Population: Adults, adolescents and young adults (12–25), older adults, with AUD, high-risk drinking, binge drinking, or other drinking exceeding limits of Canadian LRDG</li> <li>• Study types: Systematic reviews, meta-analyses, clinical trials, quasi-experimental studies, guidelines</li> <li>• Language: English</li> <li>• Year: 2000–forward</li> </ul>	<ul style="list-style-type: none"> <li>• Incarcerated populations</li> <li>• Non-English language publications</li> <li>• Opinion, letter to the editor, narrative review</li> </ul>
3. What are the harms associated with longer-term benzodiazepine prescribing in people with AUD (i.e., prescribing benzodiazepines for longer than the withdrawal period)?	<ul style="list-style-type: none"> <li>• Intervention: Benzodiazepines</li> <li>• Comparator: Placebo, alcohol use disorder pharmacotherapies (e.g., naltrexone, acamprosate, gabapentin, topiramate)</li> <li>• Outcome: Side effects, harms, or adverse events related to longer-term benzodiazepine use</li> <li>• Population: Adults, adolescents and young adults (12–25), older adults, with AUD, high-risk drinking, binge drinking, or other drinking exceeding limits of Canadian LRDG</li> <li>• Study types: Systematic reviews, meta-analyses, clinical trials, quasi-experimental studies, guidelines</li> <li>• Language: English</li> <li>• Year: 2000–forward</li> </ul>	<ul style="list-style-type: none"> <li>• Studies that focus on short-term (5-7 days) benzodiazepine prescribing for withdrawal management (detox)</li> <li>• Incarcerated populations</li> <li>• Non-English language publications</li> <li>• Opinion, letter to the editor, narrative review</li> </ul>

Limitations:

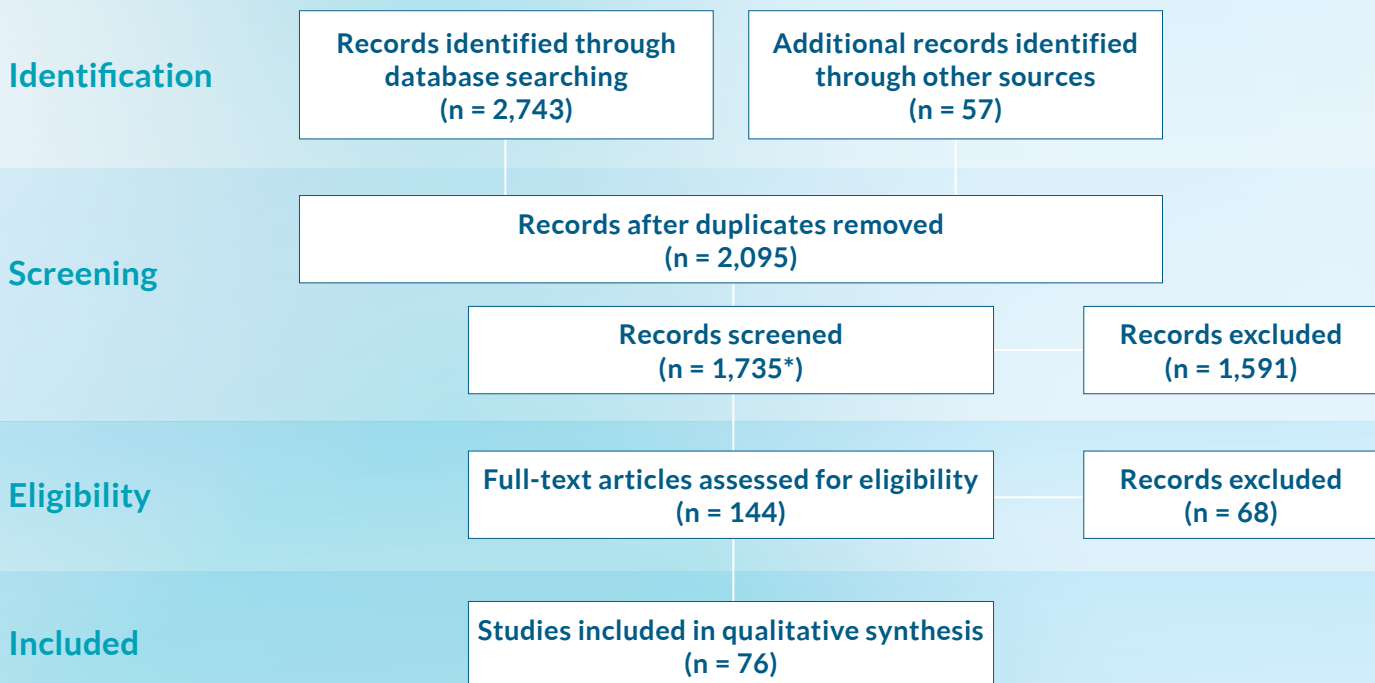
- Grey literature resources were not searched for this phase of the literature search.
- Unpublished studies and clinical trial registries were not searched.

Table 8. Items Identified by Database or Resource Type (2022 Prescribing Patterns Update Only)

Database Name	Number of items Identified	Number of items (Duplicates Removed)
Medline	655	650
CDSR	10	6
EMbase	1,743	1,316
CINAHL	238	48
PsycINFO	97	18
<b>Total – All Sources</b>	<b>2,743</b>	<b>2,038</b>

Records were deduplicated against the results from the full 2018 and updated 2020 literature searches. A total of 1,678 records remained.

## PRISMA Flow Chart – May 2022 Literature Search

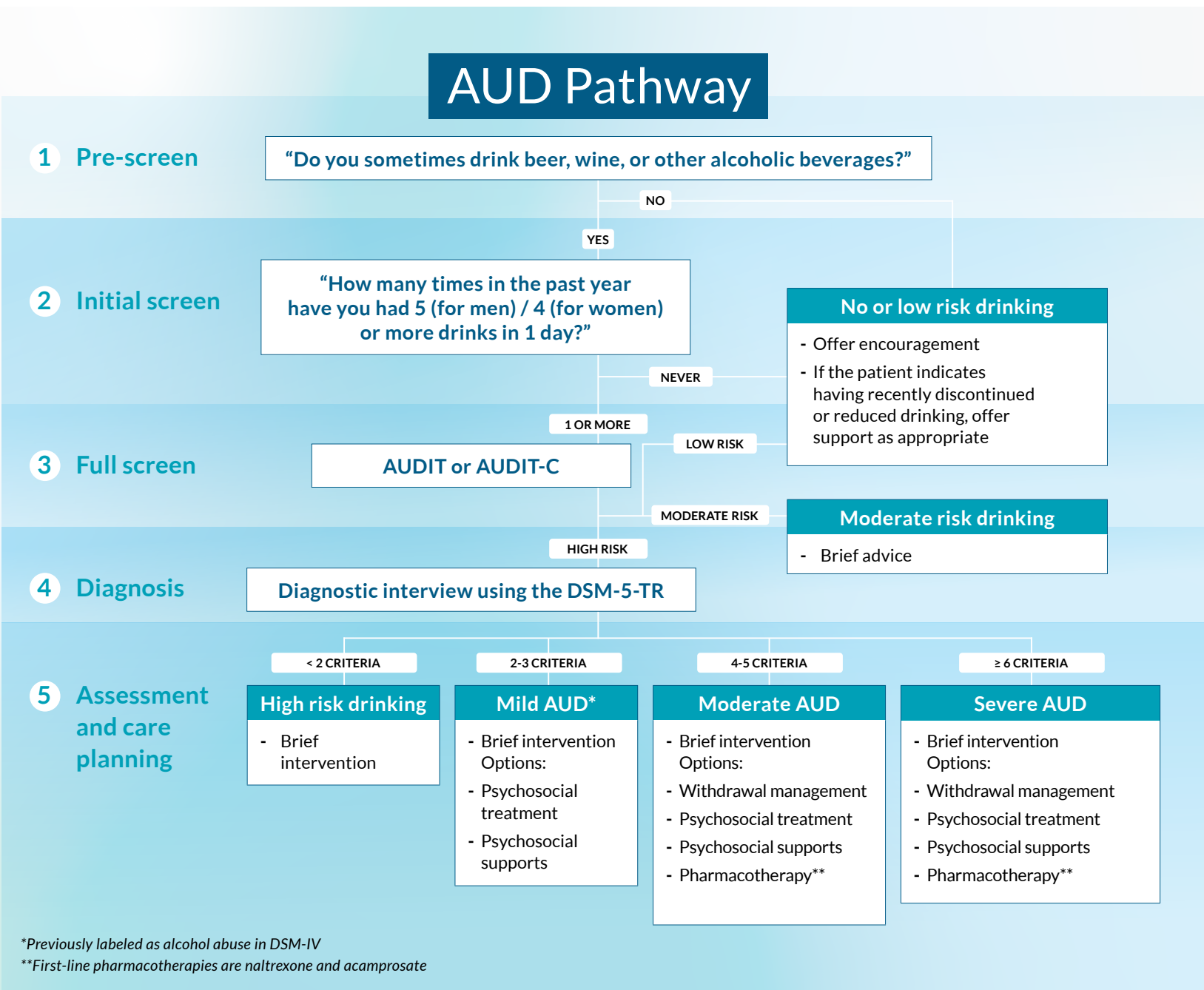


\*Only new records that were not included in the initial 2018 and subsequent 2020 literature search were screened.

# Appendix 2: Screening and Diagnosis

Universal alcohol use screening of adult and youth patients has a significant role in health promotion, as the identification of high-risk alcohol use facilitates the prevention of the wide range of alcohol-related conditions as well as AUD. This appendix provides an instructive overview of the screening and diagnosis process as depicted in Figure 1.

Figure 1. Screening, Diagnosis, and Treatment Pathway



## A2.1 Pre-Screen: Starting the Conversation (Step 1)

Introducing the topic of alcohol use to patients in a non-judgmental, conversational, and clear manner can foster a candid conversation and improve the accuracy of self-reported alcohol use. The following strategies are recommended to establish comfort and trust prior to beginning screening questions. However, it should be noted that creating trust with a patient may take more than one visit, and patient education does not have to be tied to patient disclosure of current substance use. A discussion of confidentiality and consent is needed, with the understanding that the patient may opt not to discuss their current substance use or may choose to discuss it at a subsequent appointment.

### A2.1.i Seek informed consent and discuss the confidentiality of the conversation with the patient

A patient may choose not to share information about their alcohol use for a variety of reasons (e.g., previous experiences of stigma or discrimination). In order to support patients to make an informed choice and to help build an effective therapeutic relationship, it is important to:

- Share with the patient what their rights are (e.g., to not answer certain questions) before asking the patient's permission prior to screening.
- Discuss the confidentiality of the information they share (e.g., that it will be included in their chart or electronic medical record, which is accessible to other members of the care team, but cannot be shared beyond the care team without patient permission).
  - It may be appropriate for clinicians to tell the patient that other health care providers in the patient's circle of care can access relevant medical records without the patient's consent. Clinicians may also share with patients the circumstances in which it is mandatory for health care providers to disclose a patient's medical information without the patient's consent.

- Ensure that the patient knows they can choose not to disclose information about alcohol use. In situations where the patient chooses not to disclose information about alcohol use, the clinician should answer any questions about alcohol use or health that the patient may pose in a general or hypothetical manner.
- Emphasize that you regularly ask your patients about alcohol use.
- Provide options for how to talk about alcohol use. For example, if a patient is not comfortable disclosing their own current use, they may wish to ask questions or discuss a hypothetical situation.
- Ask open-ended or exploratory questions to establish a non-judgmental and respectful tone.

Sample scripts:

*"I talk to all of my patients about alcohol and other substance use. Would it be alright for us to talk about this now?"*

If yes:

*"How does alcohol fit in your life?"*

*"What kind of relationship do you have with alcohol?"*

*"Do you sometimes drink wine, beer, or other alcoholic beverages?"*

### **A2.1.ii Use Canada's Guidance on Alcohol and Health as a communication tool**

Briefly reviewing *Canada's Guidance on Alcohol and Health* can help guide conversations toward alcohol use screening. Clinicians should clarify what is meant by "alcoholic beverages" and standard drink sizes.

Sample script:

*"Canada has guidance about drinking and its impacts on health. Would you be interested in hearing their recommendations? I try to inform all of my patients on how to prevent health issues related to alcohol."*

## A2.2 Initial Screen for High-Risk Alcohol Use in Adults (Step 2)

This guideline suggests using the single alcohol screening question (SASQ) to screen for high-risk alcohol use in adults. Prior to asking the screening question, clinicians may want to continue checking for consent and comfort.

Sample script:

*“Do you mind if I ask you some questions about how much you drink?”*

### A2.2.i Single Alcohol Screening Question (SASQ)

*“In the past year, how often have you consumed more than 4 drinks (women) or 5 drinks (men) on any one occasion?”*

#### Patient Response: never or zero times

**Interpretation:** no or low risk alcohol use

**Follow-up:**

- Offer encouragement
- Review the risk zones and situations where alcohol use should be reduced or avoided:
  - In older adults (> 65 years of age)
  - When driving, at work, and caring for children or other dependents
  - When taking medications or using substances that interact with alcohol, including other CNS depressants (e.g., opioids, benzodiazepines)
  - If patient has a health condition that could be exacerbated by alcohol
- For pregnant patients, recommend abstinence
- If patient reports no alcohol use, ask about their alcohol use history
  - Ask patient: “Was there ever a time in your life when you drank alcohol?”
- For patients with a personal or family history of AUD who have reduced or discontinued alcohol use, ask about their progress and offer encouragement and support as needed
- Re-screen annually or more frequently if clinically indicated (see [Clinical Indications for Alcohol Use Screening](#))

#### Patient Response: one or more times

**Interpretation:** possible high-risk drinking or AUD

**Follow-up:**

- Use an additional screening tool to assess for high-risk drinking (see below).



## A2.3 Full Screen for High-Risk Alcohol Use (Step 3)

For patients who are identified to potentially have high-risk alcohol use based on the SASQ, following up with a more thorough screen is recommended to increase accuracy. Several commonly used screening tools—the AUDIT-Consumption (AUDIT-C), the Alcohol Use Disorders Identification Test (AUDIT), and the Cut-down, Annoyed, Guilty, Eye Opener (CAGE) tool—are described briefly below and summarized in [Table 9](#). AUDIT-C is suggested due to its brevity, but clinicians can use their preferred screening tool. For youth patients, the NIAAA screening tool and the Car, Relax, Alone, Forget, Friends, Trouble (CRAFFT) tool are described below. When indicated and feasible, working through more comprehensive screening questionnaires together can also provide patients the opportunity to reflect on their drinking and the impact it may have on their life. The care provider should also provide feedback and answer any questions the patient may have regarding alcohol use.

### A2.3.i The Alcohol Use Disorders Identification Test (AUDIT/AUDIT-C)

The AUDIT (see [Box 10](#)) was developed by the World Health Organization (WHO) to assist in the early identification of hazardous<sup>bb</sup> or harmful<sup>bc</sup> alcohol consumption and is one of the most widely studied alcohol use screening tools. The AUDIT is also frequently used as a reference standard for the evaluation of other alcohol use screening tools. The AUDIT consists of 10 questions that assess alcohol consumption, symptoms of AUD, and alcohol-related harms. Each question is assigned a score of 0 to 4 that corresponds to frequency of occurrence, resulting in a total score ranging from 0 to 40 points. The condensed AUDIT-C (see [Box 11](#))

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bb Hazardous use: A pattern of alcohol use that increases the risk of harmful physical or mental health consequences as well as social consequences for the individual. Hazardous use occurs in the absence of an alcohol use disorder.

bc Harmful use: A pattern of alcohol use associated with the development of health consequences that cause damage to health. Damage may be physical or mental. Harmful use commonly, but not invariably, has adverse social consequences, but social consequences alone are not sufficient to justify a diagnosis of harmful use. Harmful use occurs in the absence of an alcohol use disorder.

tool consists of 3 questions about alcohol consumption and results in a total score ranging from 0 to 12. Total scores for both the AUDIT and AUDIT-C can be divided into low-, moderate-, and high-risk categories, though the AUDIT manual notes that further research is necessary to better guide the interpretation of scores and subsequent treatment planning.<sup>158,953</sup>

The 10-item AUDIT takes approximately 3 minutes to administer or complete, while the 3-item AUDIT-C requires approximately 1–2 minutes to administer or complete. Using a cut-point of 8,<sup>bd</sup> the AUDIT has an estimated sensitivity of 97% and specificity of 78% for the identification of hazardous alcohol use in general primary care populations.<sup>151</sup> The AUDIT-C has a sensitivity of 86% and specificity of 78% for the identification of hazardous alcohol use in general primary care populations using sex-specific cut points (women: 3, men: 4).<sup>151</sup> The AUDIT and AUDIT-C have been validated in a range of practice settings, including primary care clinics, assessment and emergency rooms, and acute care wards.<sup>149,954-959</sup> The AUDIT and AUDIT-C have also been validated across sexes, ethnicities, and age groups, including adolescents (aged 11–17 years), young adults (aged 18–25 years), and older adults (aged 65 years and over).<sup>167,960-964</sup> The AUDIT and AUDIT-C can be less sensitive for the identification of high-risk alcohol use in women, youth, older adults, and racialized patient populations compared to white adult men.<sup>964</sup> In line with this, a 2019 meta-analysis (N = 36, n = 50,885) found the AUDIT had differing sensitivity and specificity based on sex and country-wide prevalence of AUD. For men, a high country-wide prevalence rate of AUD was associated with a higher number of true-positives and a lower number needed to screen to treat one man with AUD, while the opposite was true for countries with a low prevalence of AUD. Overall, **the AUDIT did not accurately identify women with AUD**, producing a low true-positive rate relative to the high false-positive rate and had a wide range of numbers needed to be screened across countries (14 to 1,025).<sup>965</sup>

Time constraints, lack of experience, and the requirement to calculate scores have been cited by health care providers as barriers to more widespread uptake and use of the AUDIT and AUDIT-C in primary care.<sup>154,156,192,193</sup> As an alternative, self-administered print and electronic versions of these tools are available and can be provided to patients to complete in advance of scheduled clinical appointments

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bd Note that the original validation studies identified cut-points for hazardous/harmful alcohol use rather than low-, moderate-, and high-risk categories.

or while they are waiting to be seen. Self-administered versions of the AUDIT and AUDIT-C appear to be as effective as clinician-administered screening for the identification of hazardous or harmful alcohol use.<sup>966</sup>

Providers who elect to use the AUDIT or AUDIT-C in their practice should be aware that lower-risk limits and standard drink sizes used in these instruments are different than those used in *Canada's Guidance on Alcohol and Health*.

#### Patient Response: AUDIT: 0 to 7 or AUDIT-C: 0 to 4

**Interpretation:** Low-risk alcohol use

**Follow-up:**

- Offer encouragement
- If the patient indicates having recently discontinued or reduced drinking, offer support as appropriate
- Re-screen annually or when clinically indicated

#### Patient Response: AUDIT: 8 to 15 or AUDIT-C: 5 to 7

**Interpretation:** Moderate-risk alcohol use

**Follow-up:**

- Explore the patient's reason for consuming alcohol.
  - Ask the patient: "What does drinking do for you?"
- Provide brief advice or intervention as necessary; monitoring and follow-up
  - Brief advice can consist of providing education on the health risks associated with alcohol; discussing the benefits of reducing alcohol consumption; encouraging the patient to set goals for reducing their consumption; and providing options and tips for how to cut down
- Re-screen annually or when clinically indicated

#### Patient Response: AUDIT: $\geq 16$ or AUDIT-C: $\geq 8$

**Interpretation:** High-risk alcohol use or possible AUD

**Follow-up:**

- Explore the patient's reason for consuming alcohol.
  - Ask the patient: "What does drinking do for you?"
- Proceed to diagnosis for AUD using the DSM-5-TR criteria (Step 4).

be Detailed information and instruction on brief advice is available from the [National Health Service England](#)

Box 10. The Alcohol Use Disorders Identification Test (AUDIT)<sup>967</sup>

Read questions as written. Record answers carefully. Begin the AUDIT by saying “Now I am going to ask you some questions about your use of alcoholic beverages during this past year.” Explain what is meant by “alcoholic beverages” by using local examples of beer, wine, vodka, etc. Code answers in terms of “standard drinks”. Place the corresponding answer number in the box at the right.

<p><b>1. How often do you have a drink containing alcohol?</b></p> <p>(0) Never [Skip to Qs 9-10]            (1) Monthly or less            (2) 2 to 4 times a month            (3) 2 to 3 times a week            (4) 4 or more times a week</p>	<p><b>6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?</b></p> <p>(0) Never            (1) Less than monthly            (2) Monthly            (3) Weekly            (4) Daily or almost daily</p>
<p><b>2. How many drinks containing alcohol do you have on a typical day when you are drinking?</b></p> <p>(0) 1 or 2            (1) 3 or 4            (2) 5 or 6            (3) 7, 8, or 9            (4) 10 or more</p>	<p><b>7. How often during the last year have you had a feeling of guilt or remorse after drinking?</b></p> <p>(0) Never            (1) Less than monthly            (2) Monthly            (3) Weekly            (4) Daily or almost daily</p>
<p><b>3. How often do you have six or more drinks on one occasion?</b></p> <p>(0) Never            (1) Less than monthly            (2) Monthly            (3) Weekly            (4) Daily or almost daily</p> <p>Skip to Questions 9 and 10 if total score for Questions 2 and 3 = 0</p>	<p><b>8. How often during the last year have you been unable to remember what happened the night before because you had been drinking?</b></p> <p>(0) Never            (1) Less than monthly            (2) Monthly            (3) Weekly            (4) Daily or almost daily</p>

<p><b>4. How often during the last year have you found that you were not able to stop drinking once you had started?</b></p> <p>(0) Never  (1) Less than monthly  (2) Monthly  (3) Weekly  (4) Daily or almost daily</p>	<p><b>9. Have you or someone else been injured as a result of your drinking?</b></p> <p>(0) No  (2) Yes, but not in the last year  (4) Yes, during the last year</p>
<p><b>5. How often during the last year have you been unable to do what was normally expected from you because of drinking?*</b></p> <p>(0) Never  (1) Less than monthly  (2) Monthly  (3) Weekly  (4) Daily or almost daily</p>	<p><b>10. Has a relative or friend or a doctor or another health worker been concerned about your drinking or suggested you cut down?</b></p> <p>(0) No  (2) Yes, but not in the last year  (4) Yes, during the last year</p>
<p><b>Interpretation:</b></p> <ul style="list-style-type: none"> <li>• A score of 0–7 is considered low-risk alcohol use.</li> <li>• A score of 8–15 is considered moderate-risk alcohol use.</li> <li>• A score of 16 or more is considered a positive screen for high-risk drinking. Proceed to assessment and diagnosis for AUD.</li> </ul> <p>AUDIT/AUDIT-C: standard drink size = 10g of ethanol; Canada’s Guidance on Alcohol and Health: standard drink size = 13.45g of ethanol<sup>8</sup></p> <p style="text-align: right;"><b>Total score:</b></p>	

\*Wording has been slightly modified from the original tool to avoid stigmatizing language.

Box 11. The AUDIT-Consumption (AUDIT-C) Tool<sup>149</sup>

<p><b>1. How often do you have a drink containing alcohol?</b></p> <p>(0) Never (1) Monthly or less (2) 2 to 4 times a month (3) 2 to 3 times a week (4) 4 or more times a week</p>	<input type="text"/>
<p><b>2. How many units of alcohol do you drink on a typical day when you are drinking?</b></p> <p>(0) 1 or 2 (1) 3 or 4 (2) 5 or 6 (3) 7, 8, or 9 (4) 10 or more</p>	<input type="text"/>
<p><b>3. How often do you have six or more drinks on one occasion?</b></p> <p>(0) Never (1) Less than monthly (2) Monthly (3) Weekly (4) Daily or almost daily</p>	<input type="text"/>
<p>Interpretation: In men, a score of 4 or more is considered positive for hazardous drinking. In women, a score of 3 or more is considered positive for hazardous drinking. If score is positive, proceed to diagnosis and assessment for AUD.</p>	<p><b>Total score:</b> <input type="text"/></p>

## A2.3.ii The Cut-down, Annoyed, Guilty, Eye Opener (CAGE) Tool

CAGE is a mnemonic device that stands for “**C**ut-down, **A**nnoyed, **G**uilty, and **E**ye-opener.”<sup>968</sup> The CAGE tool is frequently used in primary care due to its brevity, ease of recall, and sensitivity for detection of AUD. The CAGE tool consists of four yes/no questions.

### Box 12. The CAGE Tool<sup>968</sup>

1. Have you ever felt you ought to <b>C</b> ut down on your drinking?
2. Have people <b>A</b> nnoyed you by criticizing your drinking?
3. Have you ever felt bad or <b>G</b> uilty about your drinking?
4. Have you ever had a drink in the morning ( <b>E</b> ye-opener) to steady your nerves or get rid of a hangover?

At a cut-point of 2 or more “yes” responses, the CAGE has an estimated sensitivity of 84% and specificity of 85% for the detection of AUD in primary care patients.<sup>151</sup> Some studies have reported that the CAGE has a lower sensitivity in youth, non-white, female, and older patient populations than in adult white men.<sup>969-972</sup> Despite its lower sensitivity among older adults compared to younger adults, only the CAGE appears to be as effective as more complex tools (e.g., the Michigan Alcohol Screening Test or MAST) for identifying AUD in older adults and due to its relative brevity, the CAGE may be more practical to administer in routine clinical practice.<sup>973,974</sup>

As a standalone screening tool, the CAGE is less sensitive and specific than the SASQ and the AUDIT/AUDIT-C for detecting AUD. Using the SASQ followed by the CAGE increases the overall sensitivity for detection of AUD to over 90% and only requires an average of 3–4 questions to be asked per patient.<sup>148</sup>

Table 9. Comparison of Selected Alcohol Use Screening Tools (Adults)<sup>151</sup>

Tool	Outcome	SE (%)	SP (%)	Comments
SASQ	High-risk drinking	84	78	<p>Provider-administered in &lt; 1 min</p> <p>Designed for use in a busy primary care setting</p> <p>Less effective for detection of high-risk drinking and AUD than more complex screening tools on its own, but can be combined with another tool to reduce likelihood that cases will be missed</p>
	AUD	88	67	<p>Well suited for a general primary care population, where most patients will not screen positive</p>
AUDIT	Hazardous drinking	97	78	<p>Self- or provider-administered in 3–4 min</p> <p>Well studied, has been validated in multiple settings and patient populations</p> <p>Less sensitive in women, youth, older adults, and racialized patient populations compared to white adult men</p>
	Harmful drinking	95	85	<p>Uses different standard drink sizes and daily drink limits than Canada’s Guidance on Alcohol and Health</p> <p>Requires provider scoring (or an electronic health record (EHR) system or other tool to compute scores)</p>
AUDIT-C	Hazardous drinking	86	78	<p>Self- or provider-administered in 1–2 min</p> <p>Well-studied, has been validated in multiple settings and patient populations</p> <p>Less sensitive in women, youth, older adults, and racialized patient populations compared to white adult men<sup>964</sup></p> <p>Uses different criteria and standard drink sizes than Canada’s Guidance on Alcohol and Health</p> <p>Requires provider scoring (or an EHR system or other tool to compute scores)</p>
CAGE	AUD	84	85	<p>Self- or provider-administered in &lt; 2 min</p> <p>More effective for identifying moderate to severe AUD than mild AUD or high-risk drinking</p> <p>Not useful as a standalone screening tool, as patients with high-risk drinking could be missed</p> <p>Less sensitive in women, youth, and racialized patient populations compared to white adult men<sup>975</sup></p> <p>Can be used as a follow-up screening tool when patients screen positive to SASQ</p> <p>Well suited for general primary care population, where most patients will not screen positive</p>



### A2.3.iii Alcohol Use Screening in Youth Patients

This guideline recommends using the NIAAA youth screening tool for youth patients (aged 11–18 years). Additional validated screening tools can be used at the discretion of the treating clinician to clarify risk if responses to the NIAAA screening questions are unclear or inconsistent with clinical signs and symptoms of alcohol use. A commonly used substance use screening tool for youth (aged 12–21)—the CRAFFT—is described briefly below. Performance characteristics for use of the NIAAA screening tool, the CRAFFT, and the AUDIT in youth are also summarized in [Table 10](#).

#### A2.3.iii.1 The NIAAA Youth Screening Tool<sup>170</sup>

The NIAAA tool is designed to identify youth (aged 11–18 years) who are at increased risk of alcohol-related problems, including AUD. The screening questions are presented below. For youth aged 11–14 (Grades 6–8), it is recommended to first ask about alcohol use among friends as a less intimidating introduction to the topic, followed by personal use questions (i.e., question 1 then 2). For patients aged 14–18 (Grades 9–12), the screening questions should be asked in reversed order (i.e., question 2 then 1).

1. *“Have any of your friends consumed alcohol in the past year?”*
2. *“Have you consumed any alcohol in the past year?”*

**If a patient reports that they do not consume alcohol:**

- Offer encouragement and reinforce healthy choices.
- Elicit and affirm the patient's reasons for not consuming alcohol.
- Offer education on the effects of alcohol for youth.
- If the patient's friends drink:
  - Ask how the patient views or feels about their friends' drinking.
  - Explore how your patient plans to stay alcohol free when friends drink.
  - Advise against riding in a car with a driver who has used alcohol or other drugs.
  - Rescreen at next visit.
- If friends do not drink:
  - Provide support for the patient's choices, social circle, and activities.
  - Rescreen annually.

### If patient reports drinking:

- Ask patient to estimate the number of drinking days they have had in the past year and assess risk based on the following thresholds:

Age	High-risk threshold for past year drinking
11 years	1 day
12–15 years	6 days (about every other month)
16 years	12 days (about monthly)
17 years	24 days (about twice monthly)
18 years	52 days (about weekly)

- For all patients who are consuming alcohol:
  - Highlight the risks of alcohol use, particularly at a time when brain development is ongoing.
  - Recommend to wait until they are of legal age to consume alcohol and offer advice on safe ways to reduce drinking.
  - Reinforce any strengths and healthy decisions.
  - Explore the potential influence of friends who drink and advise on how to mitigate those influences.
  - Ask why they drink and what benefits or what effects alcohol has for them.
  - Offer to answer any questions they have about alcohol and how it impacts health.
  - Provide support and referrals if mental health issues, trauma, or abuse are disclosed.
- For patients who drink less than their age-specific high-risk threshold:
  - For those experiencing alcohol-related problems, consider brief intervention to support a reduction or discontinuation of alcohol use (see [Appendix 3: Brief Intervention for High-Risk Alcohol Use and AUD](#)).
  - Follow up at the next visit.
- Patients who drink at or above their age-specific high-risk threshold:
  - Are at increased risk of AUD. Proceed to assessment and diagnosis (Step 4).

### A2.3.iii.2 The Car, Relax, Alone, Forget, Friends, Trouble (CRAFFT) Screening Tool<sup>976</sup>

The CRAFFT instrument is one of the most widely used screening tools in North America for the assessment of alcohol and substance use in youth aged 12–21.<sup>241,977,978</sup> An answer of “yes” to 2 or more of the 6 Part B CRAFFT questions has a sensitivity of 80% and specificity of 86% for detecting any substance use disorder<sup>979</sup> and sensitivity of 98% (95% CI: 0.91 to 1.00) and specificity of 73% (95% CI: 0.71 to 0.76) for AUD in youth.<sup>980</sup>

#### Box 13. The CRAFFT Instrument

PART A			
During the PAST 12 MONTHS, on how many days did you:		Number of days	
1	Drink more than a few sips of beer, wine, or any drink containing alcohol? Put “0” if none.		
2	Use any marijuana (weed, oil, or hash by smoking, vaping, or in food) or “synthetic marijuana” (like “K2,” “Spice”)? Put “0” if none.		
3	Use anything else to get high (like other illegal drugs, prescription or over-the-counter medications, and things that you sniff, huff, or vape)? Put “0” if none.		
Interpretation: <ul style="list-style-type: none"> <li>• If patient answered “0” for all questions above, ask Part B “CAR” CRAFFT question only.</li> <li>• If patient answered more than “0” for any of the questions above, ask all six CRAFFT questions below.</li> </ul>			
PART B			
CRAFFT Questions – Check “NO” or “YES” in columns on right.		NO	YES
C	Have you ever ridden in a CAR driven by someone (including yourself) who was “high” or had been using alcohol or drugs?		
R	Do you ever use alcohol or drugs to RELAX, feel better about yourself, or fit in?		
A	Do you ever use alcohol or drugs while you are by yourself, or ALONE?		
F	Do you ever FORGET things you did while using alcohol or drugs?		
F	Do your FAMILY or FRIENDS ever tell you that you should cut down on your drinking or drug use?		
T	Have you ever gotten into TROUBLE while you were using alcohol or drugs?		
Interpretation: <ul style="list-style-type: none"> <li>• Two or more “YES” answers to the CRAFFT questions indicate increased risk need for further assessment.</li> </ul>			

Table 10. Comparison of Selected Alcohol Use Screening Tools (Youth)<sup>980</sup>

Tool	Outcome	SE (%)	SP (%)	Comments
NIAAA screener	High-risk use	56	92	Takes 1–2 minutes to administer and score Designed for use in busy primary care settings
	AUD	87	84	Age-specific cut-offs improve sensitivity, but can be difficult to recall from memory Less sensitive than CRAFFT for detection of AUD
CRAFFT	High-risk use	81	84	Self- or provider-administered in 3–4 minutes Screens for alcohol and drug use Validated in diverse patient populations
	AUD	98	73	Less sensitive for detection of high-risk drinking High sensitivity for detection of AUD
AUDIT	High-risk use	33	99	Self- or provider-administered in 3–4 minutes Less sensitive for detection of heavy drinking or AUD among youth compared to adult populations Uses different criteria and standard drink sizes than Canada's Guidance on Alcohol and Health Requires provider scoring (or an electronic health record [EHR] system or other tool to compute scores)

### A2.3.iv Alcohol Use Screening in Pregnancy

It is imperative that education, screening, and assessment of alcohol use in pregnancy is delivered in a balanced and non-judgmental manner to prevent unintended negative consequences, such as disengagement in care.<sup>185,827</sup> Research has shown that stigma and fear of judgment is a significant barrier to accessing and staying engaged in treatment among pregnant individuals who use substances.<sup>185</sup>

This guideline recommends use of the SASQ combined with supportive dialogue for alcohol use screening in pregnancy as described above. Structured instruments can also be used to clarify alcohol use and risk, if preferred. The AUDIT, AUDIT-C, CAGE, and CRAFFT tools have been validated in pregnant patients,<sup>371,981</sup> and additional screening instruments have been developed for use in pregnancy (e.g., TWEAK, T-ACE, Substance Use Risk Profile—Pregnancy) that are not reviewed in this guideline.<sup>982-984</sup>

For additional clinical guidance on alcohol use during pregnancy and postpartum, clinicians can refer to Screening and Counselling for Alcohol Consumption During Pregnancy guideline<sup>41</sup> issued by the Society of Obstetricians and Gynaecologists of Canada and the WHO's 2014 [Guidelines for Identification and Management of Substance Use and Substance Use Disorders in Pregnancy](#).<sup>371</sup> The [BC Centre of Excellence for Women's Health](#) also has several guides to support clinicians in engaging with pregnant individuals and their partners on alcohol use. Additional tools and resources can be found on [helpwithdrinking.ca](http://helpwithdrinking.ca).

## A2.4 Diagnosis of Alcohol Use Disorder (Step 4)

Patients who screen positive for high-risk drinking should undergo a structured interview using the DSM-5-TR criteria to assess the diagnosis and severity of AUD. Diagnosis of AUD, assessment of AUD severity, and determination of the patient's risk of complications (e.g., the development of severe withdrawal symptoms) determine subsequent steps in the treatment pathway.

Table 11. Diagnosis for Alcohol Use Disorder

DSM-5-TR Diagnostic Criteria for AUD	Example interview questions
<p><b>A. A problematic pattern of alcohol use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:</b></p>	<p><b>In the last year, ...</b></p>
<p>1. Alcohol is often taken in larger amounts or over a longer period than was intended.</p>	<p>did you drink more or for a longer time than you had originally planned to?</p>
<p>2. There is a persistent desire or unsuccessful efforts to cut down or control alcohol use.</p>	<p>did you try to cut back or stop drinking, but weren't able to?</p>
<p>3. A great deal of time is spent in activities necessary to obtain alcohol, use alcohol, or recover from its effects.</p>	<p>did you spend a lot of your time drinking or recovering from drinking?</p>
<p>4. Craving, or a strong desire or urge to use alcohol.</p>	<p>were you so preoccupied with wanting a drink that you found it hard to think about anything else?</p>
<p>5. Recurrent alcohol use resulting in a failure to fulfill major role obligations at work, school, or home.</p>	<p>did you have a hard time doing your job properly or going to school because of alcohol? Taking care of your family and home?</p>
<p>6. Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol.</p>	<p>did you keep drinking even though you knew it was causing problems in your relationships?</p>
<p>7. Important social, occupational, or recreational activities are given up or reduced because of alcohol use.</p>	<p>did you give up on activities or hobbies, or seeing friends because of drinking?</p>
<p>8. Recurrent alcohol use in situations in which it is physically hazardous.</p>	<p>did you get into dangerous situations more than once because of your drinking? Like drinking and driving, unsafe sex, other situations where you could have been hurt.</p>
<p>9. Alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by alcohol.</p>	<p>did you keep drinking even though it's making you feel depressed or anxious, or it's making a physical health problem worse?</p>
<p>10. Tolerance, as defined by either of the following:</p> <ol style="list-style-type: none"> <li>A need for markedly increased amounts of alcohol to achieve intoxication or desired effect.</li> <li>A markedly diminished effect with continued use of the same amount of alcohol.</li> </ol>	<p>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?</p>
<p>11. Withdrawal, as manifested by either of the following:</p> <ol style="list-style-type: none"> <li>The characteristic withdrawal syndrome for alcohol (refer to Criteria A and B of the criteria set for alcohol withdrawal).</li> <li>Alcohol (or a closely related substance, such as a benzodiazepine) is taken to relieve or avoid withdrawal symptoms.</li> </ol>	<p>did you ever had shaky hands, anxiety, sweating, or seizures, hours after you've stopped drinking? Do you ever have a drink to prevent those symptoms from happening?</p>
<p><i>Specify if:</i></p> <ul style="list-style-type: none"> <li><b>In early remission:</b> After full criteria for alcohol use disorder were previously met, none of the criteria for alcohol use disorder have been met for at least 3 months but for less than 12 months (with the exception that Criterion A4, "Craving, or a strong desire or urge to use alcohol," may be met).</li> </ul>	

- **In sustained remission:** After full criteria for alcohol use disorder were previously met, none of the criteria for alcohol use disorder have been met at any time during a period of 12 months or longer (with the exception that Criterion A4, “Craving, or a strong desire or urge to use alcohol,” may be met).

Specify if:

- **In a controlled environment:** This additional specifier is used if the individual is in an environment where access to alcohol is restricted.

**Code based on current severity/remission:** If an alcohol intoxication, alcohol withdrawal, or another alcohol-induced mental disorder is also present, do not use the codes below for alcohol use disorder. Instead, the comorbid alcohol use disorder is indicated in the 4th character of the alcohol-induced disorder code (see the coding note for alcohol intoxication, alcohol withdrawal, or a specific alcohol-induced mental disorder). For example, if there is comorbid alcohol intoxication and alcohol use disorder, only the alcohol intoxication code is given, with the 4th character indicating whether the comorbid alcohol use disorder is mild, moderate, or severe: F10.129 for mild alcohol use disorder with alcohol intoxication or F10.229 for a moderate or severe alcohol use disorder with alcohol intoxication.

Specify current severity/remission:

- **(F10.10) Mild:** Presence of 2–3 symptoms.
- **(F10.11) Mild, In early remission**
- **(F10.11) Mild, In sustained remission**
- **(F10.20) Moderate:** Presence of 4–5 symptoms.
- **(F10.21) Moderate, In early remission**
- **(F10.21) Moderate, In sustained remission**
- **(F10.20) Severe:** Presence of 6 or more symptoms.
- **(F10.21) Severe, In early remission**
- **(F10.21) Severe, In sustained remission**

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## A2.5 Overview of Care Planning and Further Assessments (Step 5)

### A2.5.i Care Planning

The severity of AUD will help determine the treatment plan.

<b>MILD:</b> 2-3 symptoms	<b>MODERATE:</b> 4-5 symptoms	<b>SEVERE:</b> 6 or more symptoms
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Regardless of AUD diagnosis, all patients who are drinking at high-risk levels should be administered a brief intervention and encouraged to reduce or discontinue their alcohol consumption (see [Brief Intervention for High-Risk Alcohol Use and AUD](#)).

Brief intervention alone is not effective treatment for individuals with AUD.<sup>209</sup> All patients with AUD should be offered psychosocial treatment interventions (see [Ongoing Care—Psychosocial Treatment Interventions](#)) and supports, determined by the patient's needs and goals, and the accessibility of the services. Patients who are diagnosed with moderate or severe AUD should undergo a more comprehensive medical assessment (see [Further Assessments](#)), including, as appropriate and indicated: a detailed medical, mental health, and substance use history; physical examination; laboratory investigations; and risk assessment for developing severe complications of withdrawal (i.e., seizures, delirium tremens; see [Box 16. Prediction of Alcohol Withdrawal Severity Scale](#)). The outcomes of these assessments will determine whether withdrawal management is needed or desired and if pharmacotherapy is a suitable treatment option (see [Ongoing Care—Pharmacotherapy](#)). See appendices for [Withdrawal Management](#) and [AUD Pharmacotherapy](#) for detailed information.

#### **A2.5.i.1 Informed Consent**

Seeking informed consent when initiating a treatment plan requires disclosing the relevant information that will allow the patient to make a voluntary choice to accept and consent or decline the treatment plan or intervention. More information on informed consent is available through the Canadian Medical Protective Association's [Consent: A Guide for Canadian Physicians](#) and The Canadian Nurses Protective Society's [Consent to Treatment: The Role of the Nurse](#).

The informed consent process should include a description of the proposed treatment, including potential risks and benefits, the potential impact of not initiating treatment, alternative treatment options including risks and benefits, a description of engagement with care during the intervention (e.g., follow-up visits, virtual care check-ins), a description of what indicators would indicate that the patient should seek follow-up care (e.g., worsening or no change in symptoms, emergence of intolerable side effects), and a discussion of any questions or concerns raised by the patient. This conversation should be thoroughly documented in the patient's medical record.

## A2.5.ii Further Assessments

For patients with moderate or severe AUD, further assessments should be performed prior to developing a comprehensive treatment plan, in order to determine appropriate treatments and cautions (e.g., contraindicated medications or drug–drug interactions).

Table 12. Assessment Checklist

<p><b>Withdrawal Management</b></p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Conduct physical and mental health assessment, including PAWSS, to determine appropriate setting and pathway for withdrawal management, if required, or ongoing care.</li> </ul>	<p><b>Nutritional Assessment</b></p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Conduct a nutritional assessment and advise on supplementation.</li> <li><input type="checkbox"/> Assess and provide advice to correct fluid imbalances and electrolyte deficiencies. It is recommended that all patients with AUD receive multivitamin supplementation including thiamine (100-200mg), folic acid (1mg), and vitamin B6 (2mg).</li> </ul> <p>Note: Public prescription medication coverage generally does not provide benefit coverage for over-the-counter vitamins or supplements.</p>
<p><b>Substance Use</b></p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Obtain a complete substance use history including assessment for tobacco and other substance use disorders.</li> <li><input type="checkbox"/> Identify any concurrent use of CNS depressants (e.g., opioids, benzodiazepines, Z-drugs, other sedatives).</li> </ul>	<p><b>Medications</b></p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Review patient’s dispensing record of all prescriptions, if available, to assess for potential drug–drug interactions and contraindications with co-prescribed medications, including medications that may be prescribed for withdrawal management or ongoing care.</li> </ul>
<p><b>Driving Risks</b></p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Identify and address the risk of impaired driving.</li> <li><input type="checkbox"/> Patients undergoing withdrawal management should be advised not to drive or operate machinery until treatment is complete and symptoms are resolved.</li> </ul> <p>In line with guidance from the <a href="#">Canadian Medical Protective Administration</a>, prescribers should be familiar with the <a href="#">CMA Driver’s Guide</a> and use it as a guideline when determining a patient’s fitness to drive and any duty to report,<sup>986</sup> and comply with all standards, limits, conditions, and responsibilities as set out by relevant regulatory bodies.</p>	<p><b>Laboratory Investigations</b></p> <p>The following tests may be ordered to assess general health, alcohol-related comorbidities, and other conditions that could impact treatment:</p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Complete blood count (CBC), serum electrolytes, glucose, liver function and renal function panels</li> <li><input type="checkbox"/> Pregnancy test for patients of childbearing capacity</li> <li><input type="checkbox"/> Sexually transmitted and blood-borne infection testing</li> <li><input type="checkbox"/> Electrocardiogram (ECG) for patients with cardiac disease or a history of arrhythmia or syncope</li> <li><input type="checkbox"/> Chest x-ray for patients with chronic respiratory problems or respiratory symptoms</li> </ul> <p>Note: Treatment should be initiated immediately whenever possible and should not be delayed by waiting for laboratory test results unless patient safety would be compromised.</p>

# Appendix 3: Brief Intervention for High-Risk Alcohol Use and AUD

This guideline recommends that clinicians administer a brief intervention (BI) to all adult and youth patients who screen positive for high-risk drinking to support behavioural change to reduce or discontinue alcohol consumption. Brief intervention should be offered alongside other psychosocial and pharmacological treatment interventions for individuals diagnosed with AUD. Brief intervention may incorporate principles of motivational interviewing (MI), an evidence-based counselling approach that helps individuals enhance their motivation to change.<sup>201</sup> Brief interventions are typically structured using the FRAMES approach ([Table 13](#)).<sup>201,202</sup>

## A3.1 Motivational Interviewing

It is strongly recommended that providers complete MI training to maximize the effectiveness of this intervention. This appendix provides a brief overview of MI principles and guidance on using this intervention with patients who have AUD. Motivational interviewing training programs and continuing education courses are listed in the [Resources](#) section.

### A3.1.i Principles of Motivational Interviewing

Motivational interviewing is a conversational, person-centred counselling method that seeks to empower patients to examine and address feelings of ambivalence that may impact their motivation to change. This intervention is based on the recognition that when clinicians issue directives or otherwise exert pressure (whether real or perceived) on patients to change their behaviour, this often results in pushback or resistance. By following the overarching principles of MI listed below,<sup>201,987</sup> clinicians can empower patients to define and pursue well-being in their own way.

- **Partnership:** The MI counsellor<sup>bf</sup> joins the patient as a collaborator, not an authority, to understand the patient’s individual obstacles to change and to work together to overcome them.
- **Acceptance:** In conversation, the MI counsellor consistently acknowledges and affirms the patient’s inherent worth, potential, and autonomy. This allows the MI counsellor to approach the patient with “accurate empathy”—an active, non-judgmental interest in the patient perspective, which is the key to collaborative progress toward well-being.
- **Compassion:** The MI counsellor’s ultimate concern is the patient’s safety and well-being, and understanding what that means from the patient’s perspective.
- **Evocation:** Rather than imposing a set of goals and values on the patient, the counsellor elicits from the patient their goals and how they prefer to receive help and support.

### Task 1—Active listening

Active listening strategies can help build a productive partnership with the patient. The strategies of active listening are often referred to by the mnemonic “OARS”, which stands for **O**pen questions, **A**ffirmations, **R**eflective listening, and providing **S**ummaries.<sup>987</sup>

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<sup>bf</sup> The term “MI counsellor” is used in this section to denote the clinician or staff member who is administering MI-based counselling. Motivational interviewing counsellors may include physicians, nurse practitioners, nurses, psychologists, pharmacists, social workers, staff, or volunteers who have completed appropriate training.

**Open questions:** The goal of asking open questions is to support the patient to say more. The MI counsellor's goal is for the patient to speak for at least half of the total session time. Open questions invite the patient to explore their feelings about, motivations for, and barriers to change.

Sample questions:

*"Help me understand...?"*

*"How would you like things to be different?"*

*"How would you feel about...?"*

*"How would you go about...?"*

*What is important about this for you/for you in this?"*

*"What are the good things about...and what are the less good things about it?"*

*"What do you think you will lose if you give up...?"*

*"What do you want to do next?"*

**Affirmations:** The MI counsellor should express active interest in interactions with the patient by acknowledging and amplifying actions, thoughts, and values that are noteworthy or merit credit. Such affirmations can be as simple as acknowledging that the patient made the effort to come to the appointment or recognizing the patient's willingness to persist in seeking healthy change.

Example Affirmations:

*"I appreciate that you are willing to meet with me today."*

*"You are clearly a very resourceful person."*

*"You handled yourself really well in that situation."*

*"That's a good suggestion."*

*"If I were in your shoes, I don't know if I could have managed nearly so well."*

*"I've enjoyed talking with you today."*

**Reflective listening:** Periodically provide reflective statements that repeat, paraphrase, or interpret what the patient is saying. In addition to maintaining engagement and clarity, carefully selected, timed, and worded affirmations are key to the effectiveness of MI, as they may enable the patient to reconsider a certain position or belief, and recognize contradictions, oversights, or opportunities for change.

Examples of Reflective Statements:

*“So you feel...”*

*“It sounds like you...”*

*“You’re wondering if...”*

*“On the one hand you want a better life, on the other hand you are not confident you are ready to give up old behaviours.”*

**Provide summaries:** Summaries are a specific form of reflective listening that punctuates the session and recognizes key concerns raised in the conversation. These are particularly useful in transition points—after the patient has spoken about a particular topic, has recounted a personal experience, or when the session is nearing an end. Summaries can provide a stepping stone toward change by distilling the productive aspects of the conversation. Like reflections, summaries are concise and strategically constructed to recognize problems, concerns, and desire to change. End summaries with an invitation to correct or complete a thought:

*“Did I miss anything?”*

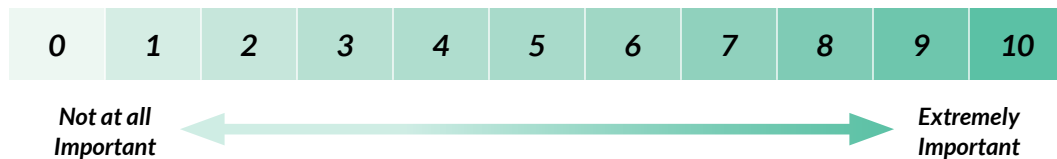
*“Is that accurate? Anything you want to add or correct?”*

## Task 2—Eliciting change talk

Active listening may enable the patient to recognize and voice their own desire and potential for change.<sup>987,988</sup> Through reflective and evocative questions, the MI counsellor can elicit and support productive thinking that reflects statements the patient makes about the need, willingness, or ability to make healthy behavioural changes.<sup>987,988</sup>

## Methods for evoking change talk<sup>988</sup>:

- Using the “importance ruler”: “How important would you say it is for you to...?”
- “On a scale of zero to ten, where zero is not at all important and ten is extremely important, where would you say you are?” This scale can also be used to gauge confidence to change.



- Exploring the decisional balance: “What do you like about your present pattern? What concerns you about it?”
- Elaborating: “What else...?”
- Exploring extremes: “What concerns you most about...?”
- Exploring goals and values: “What things are most important to you?”

## Types of change talk:

A patient’s change talk generally falls into two categories: talk in preparation of change and talk about change that is already happening.<sup>987</sup>

### Preparation

- Desire to change: “I want to get better”; “I wish I were more comfortable around people.”
- Ability to change: “I’ve been able to stop at times in the past”; “I can do this.”
- Reasons for change: “I would sleep better”; “I will feel healthier.”
- Need to change: “I can’t stand living like this anymore”; “This is worse than I thought.”

## Active change

- Commitment: “I am going to get help for this problem.”
- Actions: “I have talked to my boss about needing time off to get help.”
- Taking steps: “I have started cutting back on my alcohol use to make it easier later to stop.”

### Task 3– Collaborative planning

Once the MI counsellor establishes through OARS that they have understood the patient’s concerns and current “state of change” (e.g., through noting signifiers of preparation for change or active change), they may offer feedback and share information based on MI counsellor’s experience and expertise as requested by the patient.<sup>987</sup> Offering advice is always preceded by asking the patient’s permission, as well as inviting them to give their ideas and thoughts first.

In the course of MI, increased change talk and signs of increased motivation signal an opportunity to bridge toward planning for change. Strategic questions may prompt the patient to ask for advice; unsolicited advice should never be imposed on the patient.

The core principles of active listening (OARS) apply to all the stages of MI, including planning. The MI counsellor should move at the patient’s pace and “roll with resistance.” In response to a patient’s increased motivation for change, the MI counsellor can pose more specific and goal-oriented open questions, providing reflections and affirmations to acknowledge and mobilize motivation into planned action.

#### A3.1.ii Resources

Motivational interviewing training is available in multiple jurisdictions. A truncated list follows; clinicians are encouraged to seek out motivational interviewing training in their home communities where possible.



- [Motivational Interviewing Network of Trainers \(MINT\)](#)  
An international group of MI trainers that holds training events and provides educational material to support the effective use of MI. The MINT website features a comprehensive list of MI resources including books, educational material, and relevant articles, as well as online courses.
- [Change Talk Associates](#)  
A Vancouver-based association that provides in-person and virtual MI training and support in collaboration with the University of British Columbia Continuing Studies (UBC CS). Their website offers a list of online resources as well as the schedule of upcoming events.
- [The Centre for Addiction and Mental Health](#)  
Canada's largest mental health teaching hospital and leading research facility in the field of addiction and mental health offers an online, accredited motivational interviewing course through its continuing education program.
- [PsyMontreal](#)  
PsyMontreal provides accredited MI training to health care professionals in numerous sectors, including universities, hospitals, and social service agencies, as well as various public and private organizations across Quebec.

## A3.2 The FRAMES Model

Brief intervention approaches that adhere to the principles of MI are typically structured using the FRAMES model,<sup>201</sup> a mnemonic device that stands for **F**eedback, **R**esponsibility, **A**dvice, **M**enu, **E**mpathetic, and **S**elf-efficacy.

Table 13. The FRAMES Model for MI-Based Brief Interventions<sup>201,202</sup>

<b>Feedback</b>	<i>Provide individualized feedback on screening or assessment results. Asking open-ended questions about how the patient feels or thinks about the feedback can aid discussion.</i>
<b>Responsibility</b>	<i>Using a strengths-based, patient-centred approach, emphasize that responsibility for making the choice to change behaviour ultimately rests with the individual.</i>
<b>Advice</b>	<i>Seek permission from the patient first before giving advice. Provide clear advice that reducing or stopping alcohol use will reduce risk of future problems related to alcohol use. Many patients are unaware that their current drinking patterns could potentially lead to health or other problems, or make existing problems worse. Increased awareness of their personal risk can provide reasons to consider changing behaviour.</i>
<b>Menu</b>	<i>Review a “menu” of different options for reducing or stopping alcohol use and encourage the patient to choose the strategies that best fit their values, preferences, circumstances, and needs. Providing choice reinforces a patient’s sense of control and responsibility and can strengthen motivation to change. Using a shared decision-making framework, encourage the patient to set goals that are realistic and meaningful to the patient.</i>
<b>Empathetic</b>	<i>Use a warm, empathetic counselling style, which involves listening, understanding, and reflecting that understanding back to the patient (e.g., “reflective listening”), and is associated with improved BI outcomes.</i>
<b>Self-Efficacy</b>	<i>Encourage and reinforce the patient’s self-efficacy and confidence in their ability to change. Individuals who believe that they can make changes are much more likely to do so than those who feel powerless or helpless to change their behaviour.</i>

## A3.3 The 5A's Model for Brief Alcohol Interventions

The 5A's model is widely used in primary care and other clinical settings to support behavioural change, including dietary changes, exercise plans, smoking cessation, and substance use.<sup>106,204</sup> Guidance for adapting the 5A's approach as a brief alcohol intervention is provided below.<sup>989-991</sup>



<b>Ask</b>	<ul style="list-style-type: none"> <li>Initiate a conversation about the patient's alcohol use</li> <li>Proceed with screening and diagnosis as described in <a href="#">Appendix 2: Screening and Diagnosis</a></li> </ul>
<b>Advise</b>	<ul style="list-style-type: none"> <li>Clearly describe the screening result</li> <li>Discuss the implications on the patient's health</li> <li>Connect the health risks to the laboratory investigations and medical findings (e.g., anxiety, insomnia, liver function tests, gastroesophageal reflux disease, blood pressure), if relevant</li> <li>Discuss the patient's health concerns and goals</li> <li>Provide personalized recommendations</li> </ul> <p>Sample questions:</p> <ul style="list-style-type: none"> <li>"I think your drinking is putting your health at risk and is not good for you. What health goals are most important for you?"</li> <li>"I strongly recommend that you cut down or stop drinking. What has worked for you in the past?"</li> </ul>
<b>Assess</b>	<ul style="list-style-type: none"> <li>Assess the patient's motivation and interest in changing their drinking</li> </ul> <p>Sample questions:</p> <ul style="list-style-type: none"> <li>"Are you interested in or considering making changes in your drinking?"</li> <li>"What would you lose or gain by cutting back on your drinking?"</li> <li>"On a scale of 1 to 10, how important is it to you to cut down your drinking?"</li> <li>"How do you feel about my recommendation? Do you have any questions or concerns?"</li> </ul>

<p><b>Assist</b></p>	<p>If patient expresses readiness to change:</p> <ul style="list-style-type: none"> <li>• Express your support and offer encouragement</li> <li>• Affirm your confidence in patient’s motivation and ability to change</li> <li>• Collaboratively set goals that are meaningful to the patient. Goals do not have to be limited to reducing or stopping alcohol use and can include safer alcohol consumption</li> <li>• In line with the patient’s goals, provide a menu of options, including pharmacotherapy, psychosocial interventions, and recovery-oriented and community-based supports</li> <li>• Agree on a specific plan and a change date or schedule</li> <li>• Provide referrals to other health care services, where appropriate and as indicated</li> <li>• Offer educational material and connect to social supports and community resources</li> </ul>
	<p>If patient does not express readiness to change:</p> <ul style="list-style-type: none"> <li>• Restate your concern about patient’s health</li> <li>• Ask about any barriers to change the patient may be experiencing and invite the patient to consider how these could be navigated</li> <li>• Encourage the patient to take time to reflect on the conversation</li> <li>• Reaffirm your willingness to support when patient is ready</li> <li>• Provide referrals to other health care services, where appropriate and as indicated.</li> <li>• Offer educational material and connect to social supports and community resources.</li> <li>• Follow-up. Repeat screening and brief intervention regularly</li> </ul>
<p><b>Arrange</b></p>	<ul style="list-style-type: none"> <li>• Schedule follow-up visits</li> <li>• At follow-up, document alcohol use and assess if patient has been able to meet and sustain planned goals.</li> </ul> <p>If patient has met planned intervention goal:</p> <ul style="list-style-type: none"> <li>• Congratulate, reinforce, and support continued change</li> <li>• Coordinate care with referral partners if the patient has accessed additional support. With the patient’s consent, communicate with external or community agencies on patient’s progress</li> <li>• Assess and address any comorbid medical conditions or concurrent mental health symptoms or disorders (e.g., insomnia, depression, anxiety), noting that these may improve with reduction in alcohol use</li> <li>• Encourage the patient to set new self-identified goals and schedule follow-up appointments</li> </ul>
	<p>If patient has been unable to meet planned intervention goal:</p> <ul style="list-style-type: none"> <li>• Acknowledge that change is difficult</li> <li>• Relate drinking to problems a patient may be experiencing (e.g., health, psychological, social) as appropriate.</li> <li>• If the following measures are not already being taken, consider: <ul style="list-style-type: none"> <li>- Referring patient to external or community-based resources (e.g., peer support groups)</li> <li>- Recommending the involvement of family (if appropriate and with the patient’s consent)</li> <li>- Offering pharmacotherapy, psychosocial interventions, or both to patients with AUD</li> <li>- Re-assessing or adjusting current treatment plan</li> </ul> </li> <li>• Continue to assess and address any concurrent medical conditions or co-occurring mental health symptoms or disorders (e.g., insomnia, depression, anxiety), noting that these may improve with reduction in alcohol use <ul style="list-style-type: none"> <li>- Note: Pharmacological management of depression and anxiety is less effective while the patient continues to use alcohol</li> </ul> </li> <li>• Schedule follow-up appointments</li> </ul>

## A3.4 Additional Resources on Brief Intervention

- [Public Health Agency of Canada: Videos on Supporting Behaviour Change](#)  
This set of videos provides concrete suggestions on how primary care providers can support behaviour change among their patients. They include an overview of motivational interviewing and offer specific guidance using scenarios on how to promote healthy behaviours through the 5A's (Assess, Advise, Agree, Assist, Arrange) and the 5R's (Relevance, Risks, Rewards, Roadblocks, Repetition).
- [The College of Family Physicians of Canada: Alcohol Screening, Brief Intervention, and Referral: A Clinical Guide](#)<sup>bg</sup>  
This resource provides an overview of a simple 3-step alcohol screening, brief intervention, and referral process.
- [BC Centre of Excellence for Women's Health: Doorways to Conversation: Brief Intervention on Substance Use with Girls and Women](#)  
This resource focuses on brief intervention on substance use with girls and women in the preconception and perinatal period.
- [American Academy of Family Physicians: Addressing Alcohol Use Practice Manual: An Alcohol Screening and Brief Intervention Program](#)  
This practice manual provides a systems-change approach for implementing alcohol SBI into a primary care practice.
- [Centers for Disease Control and Prevention: Planning and Implementing Screening and Brief Intervention for Risky Alcohol Use: A Step-by-Step Guide for Primary Care Practices](#)<sup>bg</sup>  
This guide provides the process and resources necessary to help staff in any primary health care setting plan and implement SBI for alcohol use.
- [NIAAA: Helping Patients Who Drink Too Much: A Clinician's Guide](#)  
This guide is written for primary care and mental health clinician with steps on how to incorporate alcohol screening and intervention into practice.
- [NIAAA: Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide](#)<sup>bg</sup>
- This guide is designed to help health care professionals quickly identify youth at risk for alcohol-related problems.

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bg Note that that these resources provide relevant information on BI, but they refer to diagnosis using the DSM-4.

# Appendix 4: Withdrawal Management

Figure 2. Withdrawal Management Pathway for Adult Patients with Moderate or Severe AUD

## Withdrawal Management Pathway for AUD

### 1 Assessment and goal setting

1. Discuss patient's treatment goals.
  2. Assess risk by administering PAWSS. Take note of past complications (e.g., seizures, DT's)
- Is withdrawal management required or patient has goal of abstinence?

NO

If PAWSS  $\geq$  4, inform patient of risks of unsupervised withdrawal.

### 2 Risk Stratification

#### Low risk of severe complications

e.g., PAWSS < 4

YES

#### High risk of severe complications

e.g., PAWSS  $\geq$  4, past seizure

### 3 Care setting

#### Outpatient care

- Patient meets criteria for outpatient care.
- Plan for regular follow-up (e.g., in clinic, virtually).

#### Inpatient care

- If contraindications to outpatient care (e.g., homelessness).

#### Inpatient care

(recommended option)

#### Outpatient care

- Only If inpatient facility is not available or not preferred.
- Plan for regular follow-up (e.g., in clinic, virtually).

### 4 Medications\*

1. Prescribe non-benzodiazepines (e.g., gabapentin)
2. Use CIWA-Ar or SAWS to assess withdrawal symptoms and to inform ongoing care.
3. Monitor for emergence of severe withdrawal and other concerns (e.g., continued alcohol use).

1. Prescribe benzodiazepines
2. Use CIWA-Ar or SAWS at initiation and during withdrawal to inform dosing (symptom-triggered).

1. Prescribe benzodiazepines as a short-term, tapered schedule over 5–7 days.
2. Use CIWA-Ar or SAWS to assess withdrawal symptoms.
3. Monitor for emergence of severe withdrawal and other concerns (e.g., continued alcohol use).

### 5 Ongoing care planning

#### Ongoing care

Withdrawal management as a standalone intervention is not recommended. Offer continued care options: psychosocial treatments, psychosocial supports, and AUD pharmacotherapy.

\* Offer oral thiamine (200mg daily) before and during withdrawal management. In inpatient settings, offer parenteral thiamine (200-300mg daily) for 5 days minimum, followed by oral thiamine.

## A4.1 Assessment Tools

### A4.1.i Clinical Institute Withdrawal Assessment of Alcohol Scale (CIWA-Ar)<sup>283</sup>

Box 14. Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised

Patient: _____ Date: _____ Time: _____	
Pulse or heart rate, taken for one minute: _____ Blood pressure: _____	
<p><b>NAUSEA AND VOMITING</b>— Ask “Do you feel sick to your stomach? Have you vomited?” Observation.</p> <p>0 no nausea and no vomiting 1 2 3 4 intermittent nausea with dry heaves 5 6 7 constant nausea, frequent dry heaves and vomiting</p>	<p><b>TACTILE DISTURBANCES</b>— Ask “Have you any itching, pins and needles sensations, any burning, any numbness, or do you feel bugs crawling on or under your skin?” Observation.</p> <p>0 none 1 very mild itching, pins and needles, burning or numbness 2 mild itching, pins and needles, burning or numbness 3 moderate itching, pins and needles, burning or numbness 4 moderately severe hallucinations 5 severe hallucinations 6 extremely severe hallucinations 7 continuous hallucinations</p>
<p><b>TREMOR</b>— Arms extended and fingers spread apart. Observation.</p> <p>0 no tremor 1 not visible, but can be felt fingertip to fingertip 2 3 4 moderate, with patient’s arms extended 5 6 7 severe, even with arms not extended</p>	<p><b>AUDITORY DISTURBANCES</b>— 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.</p> <p>0 not present 1 very mild harshness or ability to frighten 2 mild harshness or ability to frighten 3 moderate harshness or ability to frighten 4 moderately severe hallucinations 5 severe hallucinations 6 extremely severe hallucinations 7 continuous hallucinations</p>
<p><b>PAROXYSMAL SWEATS</b>— Observation.</p> <p>0 no sweat visible 1 barely perceptible sweating, palms moist 2 3 4 beads of sweat obvious on forehead 5 6 7 drenching sweats</p>	<p><b>VISUAL DISTURBANCES</b>— Ask “Does the light appear to be too bright? Is its color 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.</p> <p>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</p>

<p><b>ANXIETY</b>— Ask “Do you feel nervous?” Observation.</p> <p>0 no anxiety, at ease  1 mild anxious  2  3  4 moderately anxious, or guarded, so anxiety is inferred  5  6  7 equivalent to acute panic states as seen in severe delirium or acute schizophrenic reactions</p>	<p><b>HEADACHE, FULLNESS IN HEAD</b>— Ask “Does your head feel different? Does it feel like there is a band around your head?” Do not rate for dizziness or light-headedness. Otherwise, rate severity</p> <p>0 not present  1 very mild  2 mild  3 moderate  4 moderately severe  5 severe  6 very severe  7 extremely severe</p>
<p><b>AGITATION</b>— Observation.</p> <p>0 normal activity  1 somewhat more than normal activity  2  3  4 moderately fidgety and restless  5  6  7 paces back and forth during most of the interview, or constantly thrashes about</p>	<p><b>ORIENTATION AND CLOUDING OF SENSORIUM</b>- Ask “What day is this? Where are you? Who am I?”</p> <p>0 oriented and can do serial additions  1 cannot do serial additions or is uncertain about date  2 disoriented for date by no more than 2 calendar days  3 disoriented for date by more than 2 calendar days  4 disoriented for place/or person</p>
<p>Total <b>CIWA-Ar</b> Score: _____</p> <p>Rater’s Initials: _____</p>	
<p>Maximum Possible Score: 67</p>	
<p>The <b>CIWA-Ar</b> is not copyrighted and may be reproduced freely. The assessment for monitoring withdrawal symptoms requires approximately 5 minutes to administer. The maximum score is 67 (see instrument). Patients scoring less than 10 do not usually need additional medication for withdrawal.</p>	
<p>Sullivan JT, Sykora K, Schneiderman J, Naranjo CA &amp; Sellers EM. Assessment of alcohol withdrawal: The revised Clinical Institute Withdrawal Assessment for Alcohol Scale CIWA-Ar. <i>Br J Addict.</i> 1989;84:1353-1357.</p>	

**Interpretation:**

Score	Severity
0-10	Mild withdrawal
11-19	Moderate withdrawal
>20	Severe withdrawal



Note: Training is required to administer this tool accurately; a regular audit and feedback process is recommended to ensure intra- and inter-rater variability is within an acceptable range.<sup>992,993</sup>

This tool should be used in conjunction with best clinical judgment when making decisions on appropriate medication protocols, schedules, and dosages.

Due to the need for a clinical interview, the CIWA-Ar is not appropriate where there is a language barrier or if the patient is cognitively impaired, delirious, or displaying a decreased level of consciousness.<sup>284</sup>

## A4.1.ii Short Alcohol Withdrawal Scale<sup>285</sup>

### Box 15. Short Alcohol Withdrawal Scale (SAWS)

<b>Short Alcohol Withdrawal Scale (SAWS)</b>				
<b>Please put a tick in the boxes to show how you have been feeling for all of the following conditions in the last 24 hours.</b>				
	None (0 points per check)	Mild (1 point per check)	Moderate (2 points per check)	Severe (3 points per check)
Anxious				
Sleep disturbance				
Problems with memory				
Nausea				
Restless				
Tremor (shakes)				
Feeling confused				
Sweating				
Miserable				
Heart pounding				

Interpretation:

Score	Severity
<12	Mild withdrawal
≥12	Moderate to severe withdrawal

Note: The SAWS tool is suitable for self-assessment. It may be completed by the patient or a clinician to assess symptoms of mild to moderate alcohol withdrawal.

The SAWS may be used as a standalone tool or as a supplement to CIWA-Ar for patients who require more frequent assessment.

#### A4.1.iii Prediction of Alcohol Withdrawal Severity Scale<sup>bh</sup> (PAWSS)<sup>263</sup>

*Box 16. Prediction of Alcohol Withdrawal Severity Scale*

PART A: THRESHOLD CRITERIA – Yes or No, no point	
	Have you consumed any amount of alcohol (i.e., been drinking) <b>within the last 30 days</b> ? OR Did the patient have a positive (+) blood alcohol level (BAL) on admission?
	If the answer to either is YES, proceed to next questions.
PART B: BASED ON PATIENT INTERVIEW – 1 point each	
1.	Have you been recently <b>intoxicated/drunk</b> , within the last 30 days?

<sup>bh</sup> The language presented in the PAWSS tool above reflects the language in the original tool. Clinicians are encouraged to use non-stigmatizing clinical language or mirror the patient’s own choice of language.

2.	Have you <b>ever</b> undergone alcohol use disorder rehabilitation treatment or treatment for alcohol use disorder?* (i.e., in-patient or out-patient treatment programs or AA attendance)
3.	Have you <b>ever</b> experienced any previous episodes of alcohol withdrawal, regardless of severity?
4.	Have you <b>ever</b> experienced blackouts?
5.	Have you <b>ever</b> experienced alcohol withdrawal seizures?
6.	Have you <b>ever</b> experienced delirium tremens or DTs?
7.	Have you combined alcohol with other “downers” like benzodiazepines or barbiturates, <b>during the last 90 days?</b>
8.	Have you combined alcohol with any other substances, <b>during the last 90 days?*</b>

### PART C: BASED ON CLINICAL EVIDENCE – 1 point each

9.	Was the patient’s blood alcohol level (BAL) greater than 200mg/dL? (SI units 43.5 mmol/L) <b>OR</b> *Portable breath alcohol concentration device indicates equivalence to BAL greater than 200mg/dL <b>OR</b> *Have you consumed any alcohol in the past 24 hours?
10.	Is there any evidence of increased autonomic activity? e.g., heart rate >120 bpm, tremor, agitation, sweating, nausea

*\*Due to the common absence of a BAL the committee has added this modification. Please see next page.*

Interpretation: 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 syndrome (AWS).

A score of  $\geq 4$  suggests **HIGH RISK** for moderate to severe (complicated) AWS; prophylaxis and/or inpatient treatment are indicated.

An online version of the original (unmodified) PAWSS can be found at [MDCalc.com](http://MDCalc.com).

#### A4.1.iii.1 Remarks and Cautions

The PAWSS has not been validated in outpatient care settings, or in youth or pregnant patient populations. While this guideline endorses the usefulness of the PAWSS for risk assessment in all settings and populations, it emphasizes that, when making clinical decisions, **this tool should be used in conjunction with best**

clinical judgment based on a comprehensive assessment of a patient's medical history, current circumstances, medical, psychological, social, and cultural needs, and preferences.

#### A4.1.iii.2 Modifications

##### Question 9—Blood Alcohol Level (BAL)

The vast majority of outpatient care settings will not be equipped to assess BAL at point of care. As an alternative, the committee recommends that the PAWSS administrator ask patients:

*Have you consumed any alcohol in the past 24 hours?*

Based on rates of alcohol metabolism and elimination in humans,<sup>994</sup> it is very unlikely that a patient who has not consumed alcohol in the past 24 hours would have a BAL greater than 200mg/dL. While any alcohol consumption in the past 24 hours is a conservative measure of BAL > 200mg/dL (i.e., this low threshold may over-identify those at risk), it is the consensus of the committee that the benefits of identifying individuals at risk of severe complications outweigh the risk of false negatives for this questionnaire item.

Alternatively, if a portable breath alcohol concentration device (i.e., a “breathalyzer”) is available, breath alcohol concentration can be used in place of BAL. Research indicates that breath alcohol concentration is strongly correlated with BAL.<sup>995,996</sup>

#### A4.1.iii.3 Qualifiers

The following questionnaire items should be clearly understood by the PAWSS administrator and defined for the patient to maximize the accuracy of results.

##### Question 4—Blackouts

Blackouts are transient episodes of retrograde amnesia typically **without loss of consciousness** that accompany various degrees of alcohol intoxication.<sup>263</sup>

Blackouts can be an indicator of severe intoxication or long-term alcohol use, as a considerable degree of alcohol tolerance is required to ingest the amount of alcohol that could trigger a subsequent episode of amnesia without loss of consciousness.<sup>263</sup> The PAWSS administrator should clearly distinguish between alcohol-related blackouts and loss of consciousness (i.e., “passing out”) as they pose the question to the patient.

#### Question 5—Withdrawal Seizures

Withdrawal seizures are typically generalized brief tonic-clonic seizures that occur 6–48 hours after reduction or discontinuation of alcohol use.<sup>300</sup> Patients may mistake other experiences, such as tremor, for a seizure; it is important to define what is meant by a withdrawal seizure and differentiate it from other withdrawal symptoms. As patients with AUD are at increased risk of idiopathic epilepsy or seizure for other reasons,<sup>997,998</sup> the PAWSS administrator should clearly define withdrawal seizures as those that occur within 1–2 days of ceasing or greatly reducing alcohol use.

#### Question 6—Delirium Tremens (DTs)

Delirium tremens is a severe consequence of alcohol withdrawal that requires immediate hospitalization and management; if left untreated, the risk of death is approximately 3–5%.<sup>276</sup> Symptoms include profound disorientation, confusion, and agitation, accompanied by severe autonomic hyperactivity.<sup>276</sup> In colloquial language, delirium tremens or “DTs” has come to loosely represent general symptoms of alcohol withdrawal. The PAWSS administrator should clearly distinguish delirium tremens from other withdrawal symptoms to avoid false positive results.

## A4.2 Planning for Withdrawal Management

Before planning for withdrawal management, clinicians should assess and identify the patient’s treatment goals. If withdrawal management is desired or necessary, the PAWSS should be used to determine the risk of severe complications. Based on the PAWSS score and clinical parameters such as past seizures or delirium tremens,

clinicians can determine whether the patient meets the criteria for outpatient withdrawal management (see [Box 7](#) for full list of criteria). Inpatient withdrawal management in a hospital or specialized facility should be considered for patients who do not meet those criteria, who have any other contraindications to outpatient management as per the clinical judgment of the treating health care provider, or who express a preference for inpatient withdrawal management.

Planning for outpatient withdrawal should include relapse prevention support, as well as overdose prevention and safety planning. With the patient, collaboratively design a plan around possible triggers and what to do to seek support. Scheduling, designation of support people, instructions, nutritional supplementation, monitoring and follow-up plans should all be determined prior to beginning withdrawal. See [Box 8](#) for a detailed description of planning tasks.

#### Sample Scripts

*“What are the reasons you drink?”*

*“What do you anticipate could be a trigger as you try to stop?”*

*“What has helped you stop or cut down your drinking in the past?”*

*“How can we best support you during this withdrawal period?”*

*“This is what you can expect during the withdrawal period...”*

## A4.3 Prescribing Pharmacotherapy for Withdrawal Management

This appendix lists medications for withdrawal management; it does not stratify treatments in terms of first- and second-line options. Prescribers should select the most appropriate medication for a particular patient based on their medical history, circumstances, and preferences. Of note, while the efficacy of

benzodiazepines for withdrawal management is supported by the largest body of evidence, this guideline recommends non-benzodiazepine pharmacotherapies for outpatient withdrawal management due to their superior safety profile. Benzodiazepines can be considered for outpatients who are at a high-risk of severe complications from withdrawal in situations where inpatient services are not available or feasible. In these cases, benzodiazepines should be prescribed as a short-course and clinicians should plan to closely monitor patients for adverse events, side effects, and appropriate medication adherence.

To facilitate decision making, this appendix includes profiles of each alcohol withdrawal medication reviewed in this guideline, including sample dosing protocols. With the exception of benzodiazepines, which include Health-Canada approved medications for AUD (chlorazepate,<sup>999</sup> diazepam,<sup>1000</sup> and oxazepam<sup>1001</sup>), use of the medications reviewed below would be considered “off-label.” As with any medication that is being prescribed off-label, it is important to conduct a full assessment including carefully reviewing concomitant medications for potential drug–drug interactions, and documenting patient consent in their chart.

As comparative safety and efficacy of off-label pharmacotherapies has not been fully established in adolescent, pregnant, older adult, or more complex patient populations (e.g., concurrent medical conditions, concurrent mental health and substance use disorders), prescribing these medications would be at the clinician’s discretion following a careful assessment of risks, benefits, drug–drug interactions and contraindications (particularly for pregnant individuals). Clinicians are encouraged to consult an addiction medicine specialist for additional information and case-specific guidance, when necessary.

Contraindications, cautions, and side effects have been abstracted from clinical trials and supplemented with data from Health Canada-approved product monographs for specific clinical indications. For medications prescribed off-label, duration and dosages differ from those used for indicated conditions (e.g., seizure disorders, hypertension). Clinicians must be aware of these differences when prescribing off-label medications for alcohol withdrawal.

Table 14. Overview of Pharmacotherapy Options for Withdrawal Management

Drug Name	Benzodiazepines <sup>1000</sup>	Carbamazepine <sup>344</sup>	Gabapentin <sup>626</sup>	Valproic Acid <sup>1002</sup>	Clonidine <sup>1003</sup>
<i>Drug class</i>	<i>Benzodiazepines</i>	<i>Anticonvulsant</i>			<i>α-adrenergic agonist</i>
<b>Concurrent alcohol use</b>	<ul style="list-style-type: none"> <li>Potentiate the effects of alcohol; can lead to serious safety risks, incl. over sedation, falls, delirium, respiratory depression (e.g., non-fatal or fatal overdose), and prolonged hospitalization</li> </ul>	<ul style="list-style-type: none"> <li>No well-described safety risk</li> </ul>	<ul style="list-style-type: none"> <li>Abstinence recommended during treatment due to risk of additive CNS-depressive effects</li> <li>Note: Studies suggest at therapeutic doses gabapentin is not likely to increase sedation or motor impairment<sup>537</sup></li> </ul>	<ul style="list-style-type: none"> <li>No safety risk if taken concurrently with alcohol</li> </ul>	<ul style="list-style-type: none"> <li>Risk of additive effect on lowering blood pressure</li> </ul>
<b>Contraindications</b>	<ol style="list-style-type: none"> <li>Severe respiratory insufficiency</li> <li>Sleep apnea</li> <li>Myasthenia gravis</li> <li>Narrow angle glaucoma</li> </ol>	<ol style="list-style-type: none"> <li>Hepatic disease</li> <li>Bone marrow depression</li> <li>Serious blood disorder</li> <li>Atrioventricular heart block</li> </ol>	<ol style="list-style-type: none"> <li>Hypersensitivity to gabapentin</li> </ol>	<ol style="list-style-type: none"> <li>Mitochondrial disease</li> <li>Hepatic disease or dysfunction</li> <li>Urea cycle disorders</li> </ol>	<ol style="list-style-type: none"> <li>Sinus node function impairment</li> <li>Severe bradyarrhythmia</li> <li>Galactose intolerance</li> </ol>
<b>Cautions</b>	<ol style="list-style-type: none"> <li>Lactose intolerance</li> <li>Liver dysfunction</li> <li>Renal impairment</li> <li>Breast feeding</li> </ol>	<ul style="list-style-type: none"> <li>Associated with rare blood dyscrasias and Stevens Johnson Syndrome with long-term use</li> <li>The HLA-B*15:02 and HLA-A*31:01 alleles increase risk of carbamazepine toxicity<sup>345</sup></li> </ul>	<ul style="list-style-type: none"> <li>Renal impairment</li> </ul>	<ul style="list-style-type: none"> <li>Pregnant or intending to become pregnant</li> <li>Older adult patients (&gt; 65 years of age)</li> </ul>	<ul style="list-style-type: none"> <li>Hypotension in sensitive patients</li> </ul>



<b>Side effects</b>	<ul style="list-style-type: none"> <li>• Drowsiness, dizziness.</li> <li>• Less common: changes in skin colour, nausea, headache, blurred vision, tremors, hypotension, GI disturbances, memory loss</li> </ul>	<ul style="list-style-type: none"> <li>• Dizziness, pruritus, ataxia, headache, drowsiness, nausea (all usually minor and temporary)</li> </ul>	<ul style="list-style-type: none"> <li>• Higher doses may cause ataxia, slurred speech, drowsiness</li> <li>• Profile is better than other anticonvulsants</li> </ul>	<ul style="list-style-type: none"> <li>• Somnolence, GI disturbances, confusion, tremor</li> </ul>	<ul style="list-style-type: none"> <li>• Hypotension, dry mouth, dizziness, fatigue, headache, nausea, vomiting, constipation, malaise, sleep disorder, sedation, erectile dysfunction</li> </ul>
<b>Other considerations</b>	See the following section for a more detailed overview of each medication				
<b>Dosing</b>	See the following section for dosing information				

Table 15.

Benzodiazepines <sup>1000</sup>	
Contraindications	Severe respiratory insufficiency Sleep apnea Myasthenia gravis Narrow angle glaucoma
Cautions	Lactose intolerance Renal impairment Liver dysfunction <sup>bi</sup> Breast feeding Pregnancy Older adults Benzodiazepine use disorder
Side effects	The most common side effects of benzodiazepines are drowsiness and dizziness.  Less common side effects include changes in skin colour, nausea, headache, blurred vision, tremors, hypotension, GI disturbances, and memory loss.
Concurrent alcohol use	Potentiate effects of alcohol; can lead to serious safety risks including oversedation, falls, delirium, respiratory depression (e.g., non-fatal or fatal overdose), and prolonged hospitalization
Other considerations	<p>Potential for non-medical use, diversion, and dependence or benzodiazepine use disorder</p> <p>Potential for drug–drug interactions with CNS depressants (e.g., alcohol, opioids, benzodiazepines) and gabapentin, leading to excess sedation, impaired psychomotor and cognitive functioning.</p> <p>Controlled laboratory studies have suggested that benzodiazepine use may have a priming effect that increases motivation and use of alcohol.<sup>702</sup></p> <p>Consider a fixed dosing schedule for outpatient withdrawal management to limit risks. Benzodiazepines should be discontinued after withdrawal symptoms have resolved (typically 5–7 days).</p> <p>Patients and families should be aware of the risk of dependence and tolerance, and receive education on safe use, the signs of an overdose, and emergency contact information.</p> <p>Consider the following strategies to reduce risk: daily dispensing from a pharmacy, involving family members, friends, caregivers, or a community support person to administer medication and monitor patient response, frequent follow-up visits, or daily check-ins by phone.</p> <p>Lorazepam is preferred for those with severe respiratory or liver disease and in older adults (consider lower dosing).</p>

bi It is common for patients with severe AUD to have liver dysfunction. Patients with liver dysfunction who are at risk of developing severe withdrawal complications should be prescribed benzodiazepines for withdrawal management. Clinicians should consider a shorter-acting benzodiazepine at a lower dose for these patients.

Sample dosing protocol<sup>297,302</sup>

In inpatient and outpatient settings, benzodiazepines should be offered for a maximum of 7 days and should be tapered. Shorter durations are preferred.

Example four-day fixed and flexible protocols for diazepam (Valium)

Schedule	Day 1	Day 2	Day 3	Day 4
<b>Fixed<sup>a</sup></b>	5–10mg QID	5–10mg TID	5–10mg BID	5–10mg HS
<b>Flexible<sup>b</sup></b>	5–10mg q 4-6h PRN based on symptoms <sup>c</sup>	5–10mg q 6-8h PRN	5–10mg q 12h PRN	5–10mg HS, PRN

- a Fixed dosing is intended for outpatients and should be individually tailored to the extent possible, with adjustments made following daily check-ins.
- b Flexible dose schedules should be used in inpatient settings where close monitoring is feasible and dosage should be based on symptom severity. In outpatient settings, flexible dosing should only be used with patients with expected reliability and ability to adhere to clinical recommendations.
- c Symptoms: Pulse rate >100 beats per minute, diastolic BP > 90mmHg, or symptoms of withdrawal (e.g., shakes, anxiety, hallucinations).

For outpatients, enlisting family members or other caregivers to assess symptom severity and dispense medication is recommended.

Example four-day fixed protocol for lorazepam (Ativan)

**Day 1-2**            1–2mg q 4h  
**Day 3-4**            0.5–1mg q 4h

Table 16.

<b>Carbamazepine</b>									
<b>Contraindications</b> <sup>344</sup>	<p>Hepatic disease                      Bone marrow depression                      Serious blood disorder                      Atrioventricular heart block</p>								
<b>Cautions</b> <sup>344</sup>	<p>Associated with rare blood dyscrasias and Stevens Johnson Syndrome, which usually develops within the first few months of taking this medication.</p> <p>Onset of potentially serious blood dyscrasias may be rapid, patients should be informed of early toxic signs of a potential hematological problem.</p> <p>Patients should be advised to immediately consult their physician if they experience reactions such as fever, sore throat, rash, ulcers in the mouth, easy bruising, petechial or purpuric hemorrhage.</p> <p>The HLA-B*15:02 and HLA-A*31:01 alleles increase risk of carbamazepine toxicity. Consider monitoring patients for adverse reactions to carbamazepine if there is an elevated risk of carrying the HLA-B*15:02 or HLA-A*31:01 allele.</p>								
<b>Side effects</b> <sup>335</sup>	<p>The most commonly reported side effects are dizziness, pruritus, ataxia, headache, drowsiness, nausea. Side effects are often minor and temporary, but they can occur in up to 18% of patients.<sup>335</sup></p>								
<b>Concurrent alcohol use</b>	<p>No safety risk if used concurrently with alcohol.</p>								
<b>Other considerations</b> <sup>335,344,345</sup>	<p>No risk of non-medical use, diversion, or dependence</p> <p>Conduct a critical risk-benefit appraisal when considering carbamazepine in patients with a history of cardiac, hepatic, or renal damage; adverse hematological reactions to other drugs; or previously interrupted treatments with carbamazepine. A comprehensive clinical assessment including appropriate laboratory investigations should be conducted prior to treatment initiation.</p> <p>A CBC including platelets and possibly reticulocytes and serum iron should be requested to ensure healthy bone marrow function prior to prescribing carbamazepine. If low platelet counts are observed, the patient should be monitored closely.</p> <p>Patients should also be aware of symptoms of dermatological or hepatic reactions. In addition to baseline testing, hepatic function in older adult patients and patients with a history of liver disease must be monitored during the course of treatment.</p> <p>Prescribers should review carbamazepine's drug-drug interactions with a pharmacist or other source when considering this medication for alcohol withdrawal management.</p>								
<b>Sample Dosing Protocols</b> <sup>338-343,1004,1005</sup>	<table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 15%;"><b>Day 1</b></td> <td>200mg QID</td> </tr> <tr> <td><b>Day 2</b></td> <td>200mg TID</td> </tr> <tr> <td><b>Day 3</b></td> <td>200mg BID</td> </tr> <tr> <td><b>Day 4-5</b></td> <td>200mg OD</td> </tr> </table> <p>Note: This protocol applies to immediate-release (IR) tablets. For withdrawal management, most clinical trials have used a standard tapered 5-day regimen. There is no PRN regimen for this medication.</p>	<b>Day 1</b>	200mg QID	<b>Day 2</b>	200mg TID	<b>Day 3</b>	200mg BID	<b>Day 4-5</b>	200mg OD
<b>Day 1</b>	200mg QID								
<b>Day 2</b>	200mg TID								
<b>Day 3</b>	200mg BID								
<b>Day 4-5</b>	200mg OD								

Table 17.

Gabapentin													
Contraindications <sup>344,626</sup>	Hypersensitivity to gabapentin												
Cautions <sup>626</sup>	Renal impairment—gabapentin is eliminated solely by renal excretion. Dosage adjustments are recommended for patients with renal impairment (including older adult patients with declining renal function) and patients undergoing hemodialysis.												
Side effects <sup>626</sup>	The most common side effects are ataxia, slurred speech, and drowsiness.												
Concurrent alcohol use <sup>537,626</sup>	<p>A higher-than-therapeutic dose and concurrent alcohol or opioid use increases the risk of respiratory depression, profound sedation, syncope, and death. Patients who continue the use of alcohol or other CNS depressants should be observed closely for signs and symptoms of CNS depression, and the dose of gabapentin may need to be adjusted accordingly.</p> <p>Note: Studies suggest concomitant use of alcohol and gabapentin at therapeutic doses does not increase sedation or motor impairment.</p>												
Other considerations <sup>626</sup>	<p>Potential for non-medical use, diversion, and dependence</p> <p>Patients with compromised respiratory function, respiratory or neurological disease, renal impairment and older adults are at higher risk of experiencing severe CNS-related adverse effects, including sedation, somnolence, loss of consciousness as well as serious cases of respiratory depression.</p> <p>Gabapentin is eliminated primarily by renal excretion; dosage adjustment may be required in older adult patients and patients with renal impairment.</p> <p>Prescribers should review gabapentin’s drug–drug interactions when considering this medication for alcohol withdrawal management.</p> <p>Easy to transition from withdrawal management to ongoing AUD pharmacotherapy using gabapentin.</p>												
Sample Dosing Protocol <sup>537</sup>	<p><b>Note:</b> This protocol applies to immediate-release (IR) tablets.</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="text-align: left;">Symptoms</th> <th style="text-align: left;">Regular Dose</th> <th style="text-align: left;">PRN</th> <th style="text-align: left;">HS</th> </tr> </thead> <tbody> <tr> <td>If CIWA-Ar is 10-14 or SAWS ≥ 12</td> <td>300mg TID. Titrate up to 600mg TID if symptoms are not responding</td> <td>300mg PRN - leave 2 hrs btwn regular and PRN doses</td> <td>300-600mg HS PRN</td> </tr> <tr> <td>If CIWA-Ar is &lt; 10 or SAWS &lt; 12</td> <td></td> <td>300mg q4 h PRN</td> <td>300-600mg q HS PRN</td> </tr> </tbody> </table> <p><i>When acute symptoms resolve and CIWA &lt; 10 or SAWS &lt; 12 consistently (e.g., 3 measurements), taper over 3-5 days, reducing dose by 600mg each day</i></p> <p><i>Max daily dose is 3600mg</i></p> <p><i>Hold doses if patient shows drowsiness, ataxia, or slurred speech</i></p> <p><b>Clinical Tip:</b></p> <p>To determine whether additional gabapentin is needed for treatment of breakthrough withdrawal symptoms, patients and caregivers can be instructed to use the Short Alcohol Withdrawal Scale (SAWS; see <a href="#">Box 15</a>). Regardless of whether the patient is at 300mg or 600mg TID, additional doses of gabapentin 300mg TID PRN can be taken if SAWS scores are ≥ 12 or the patient is experiencing craving, insomnia, or irritability.</p>	Symptoms	Regular Dose	PRN	HS	If CIWA-Ar is 10-14 or SAWS ≥ 12	300mg TID. Titrate up to 600mg TID if symptoms are not responding	300mg PRN - leave 2 hrs btwn regular and PRN doses	300-600mg HS PRN	If CIWA-Ar is < 10 or SAWS < 12		300mg q4 h PRN	300-600mg q HS PRN
Symptoms	Regular Dose	PRN	HS										
If CIWA-Ar is 10-14 or SAWS ≥ 12	300mg TID. Titrate up to 600mg TID if symptoms are not responding	300mg PRN - leave 2 hrs btwn regular and PRN doses	300-600mg HS PRN										
If CIWA-Ar is < 10 or SAWS < 12		300mg q4 h PRN	300-600mg q HS PRN										

Table 18.

Clonidine	
Contraindications <sup>344,1003</sup>	Sinus node function impairment Severe bradyarrhythmia Galactose intolerance Syncope attributable to hypotension
Cautions <sup>1003</sup>	May cause hypotension in patients with a history of low blood pressure.
Side effects <sup>1003</sup>	Hypotension, dry mouth, dizziness, fatigue, headache, nausea, vomiting, constipation, malaise, sleep disorder, sedation, and erectile dysfunction.
Concurrent alcohol use <sup>1003</sup>	Clonidine and alcohol can have additive effects in lowering blood pressure. If consumed together, patients may experience headache, dizziness, light-headedness, fainting, or changes in pulse or heart rate.
Other considerations <sup>359,362,1003</sup>	As a standalone treatment, clonidine should only be used for treating mild withdrawal symptoms in patients at low risk of severe complications (PAWSS < 4).  Safe to use with benzodiazepines or other anticonvulsants (gabapentin, carbamazepine, valproic acid) as an adjunct treatment for alcohol withdrawal.  Patients and families should receive education on the signs and symptoms of hypotension.
Sample Dosing Protocol <sup>360,362</sup>	<p><b>Start</b></p> <p>0.1-0.2mg BID (last dose at HS)</p> <p><b>Titrate</b></p> <p>Can add 0.2mg OD PRN</p> <p><b>Final Dose</b></p> <p>0.1-0.6mg BID</p> <p>To ensure blood pressure control during sleep, it is recommended that the last dose of the day be taken immediately before going to sleep.</p>

Table 19.

Valproic Acid	
Contraindications <sup>344,1002</sup>	Mitochondrial disease Hepatic disease or dysfunction Urea cycle disorders
Cautions <sup>1002</sup>	Pregnant patients or patients intending to become pregnant Older adults (≥65 years)
Side effects <sup>1002</sup>	The most common side effects are hypotension, dry mouth, dizziness, fatigue, headache, nausea, vomiting, constipation, malaise, sleep disorder, sedation, and erectile dysfunction.
Concurrent alcohol use <sup>1002</sup>	No significant safety risk if taken concurrently with alcohol.
Other considerations <sup>1002</sup>	<p>Due to limited evidence of efficacy, valproic acid should be considered only when all other withdrawal pharmacotherapy options are contraindicated.</p> <p>Extreme caution should be exercised when considering valproic acid for pregnant patients or individuals with childbearing capacity due to the risk of dose-dependent teratogenic effects such as spina bifida.</p> <p>Conservative dosing is recommended for older adults (≥65 years of age.)</p> <p>Prescribers should review valproic acid's drug–drug interactions when considering this medication for alcohol withdrawal management.</p>
Sample Dosing Protocol <sup>1006,1007</sup>	<p><b>If CIWA &lt;10 prior to treatment:</b></p> <p><b>Day 1–5</b>      Start at 250mg TID x 5 days If withdrawal symptoms persist, titrate to 500mg TID x 1-3 days Once stabilized, reduce to 250mg for days 4–5</p> <p><b>Day 6</b>      Discontinue medication</p> <p><b>If CIWA ≥10 prior to treatment:</b></p> <p><b>Days 1–3</b>      Start at 500mg TID</p> <p><b>Days 4–5</b>      Reduce to 250mg TID</p> <p><b>Day 6</b>      Discontinue medication</p> <p><b>Note:</b> Published dosing protocols for valproic acid use symptom-triggered schedules based on CIWA-Ar score (see <a href="#">Box 14</a>).</p>

# Appendix 5: AUD Pharmacotherapy

Prior to initiating pharmacotherapy, [assessments](#) should be performed to determine medication contraindications and possible drug-drug interactions. This guideline recommends naltrexone and acamprosate as first-line pharmacotherapies for AUD. In addition to other individual factors (e.g., contraindications, coverage), selection between these medications depends on the patient’s treatment and recovery goals. Naltrexone is recommended for patients with a goal of abstinence or reduced drinking, and acamprosate is recommended for patients who have a goal of abstinence. This appendix provides dosing instructions and practical considerations to facilitate treatment selection and administration.

This appendix also offers information to support selection of alternative pharmacotherapies—topiramate, gabapentin, and disulfiram—if first-line medications are contraindicated, not effective, or not preferred. With the exception of disulfiram, which is a Health Canada-approved medication for AUD, use of these alternative medications would be considered “off-label.” As with any medication that is being prescribed off-label, it is important to conduct a full assessment including carefully reviewing concomitant medications for potential drug-drug interactions, and documenting patient consent in their chart. [Table 24](#) provides a visual comparison of the recommended medications.

As comparative safety and efficacy of AUD pharmacotherapies has not been fully established in adolescent, pregnant, older adult, or more complex patient populations (e.g., concurrent medical or mental health conditions), prescribing these medications in these cases would be at the clinician’s discretion following a careful assessment of risks, benefits, drug-drug interactions, and contraindications. Clinicians are encouraged to consult an addiction medicine specialist for additional information and case-specific guidance, when necessary.

Contraindications, cautions, and side effects have been abstracted from clinical trials and supplemented with data from Health Canada-approved product monographs for specific clinical indications. Duration and dosages used for indicated conditions (e.g., seizure disorders) may differ from those used off-label for AUD treatment. Data should be interpreted cautiously with this in mind.



## A5.1 First-line AUD Pharmacotherapies

Table 20. First-line AUD Pharmacotherapies (Naltrexone and Acamprosate)

	Naltrexone <sup>492</sup>	Acamprosate <sup>624</sup>
<b>Concurrent alcohol use</b>	<ul style="list-style-type: none"> <li>No well-described safety risk</li> </ul>	<ul style="list-style-type: none"> <li>No well-described safety risk</li> </ul>
<b>Contraindications</b>	<ol style="list-style-type: none"> <li>Naltrexone hypersensitivity</li> <li>Any current opioid use (prescription or non-medical)</li> <li>Acute opioid withdrawal</li> <li>Acute hepatitis or liver failure</li> </ol>	<ol style="list-style-type: none"> <li>Acamprosate hypersensitivity</li> <li>Severe renal impairment (creatinine clearance <math>\leq</math> 30mL/min)</li> <li>Breastfeeding</li> </ol>
<b>Cautions</b>	<ol style="list-style-type: none"> <li>Renal impairment</li> <li>Severe hepatic impairment</li> <li>Concomitant use of other potentially hepatotoxic drugs</li> <li>Pregnancy and breastfeeding*</li> <li>Pediatric patients (&lt; 18 years)*</li> </ol>	<ol style="list-style-type: none"> <li>Moderate renal impairment (creatinine clearance of 30–50mL/min)</li> <li>Pediatric and geriatric (&gt; 65 years) patients*</li> <li>Pregnancy*</li> </ol>
<b>Side effects</b>	<ul style="list-style-type: none"> <li>Nausea, headache, and dizziness</li> <li>Generally mild and temporary</li> <li>Starting at low dose and/or abstinence from alcohol can reduce side effects</li> </ul>	<ul style="list-style-type: none"> <li>Diarrhea, vomiting, and abdominal pain</li> <li>Side effects are usually transient and resolve quickly</li> </ul>
<b>Coverage and Cost</b>	The cost of naltrexone and acamprosate will vary by coverage and jurisdiction. Consult the regional drug formulary for details.	
<b>Safety and other considerations</b>	<ul style="list-style-type: none"> <li>Liver function tests (LFTs) at initial treatment, and 1, 3, and 6 months. More frequent monitoring if LFTs are elevated</li> <li>Due to risk of hepatic injury, advise patients to stop treatment if signs of acute hepatitis appear (fatigue, anorexia, nausea, and vomiting)</li> </ul>	<ul style="list-style-type: none"> <li>No safety risk with mild renal impairment (creatinine clearance 50–80mL/min)</li> <li>Moderate impairment (creatinine clearance 30–50mL/min) requires dose reduction<sup>31</sup></li> <li>No hepatic toxicity</li> </ul>

## Dosing

Naltrexone can be prescribed as OD or PRN. As-needed (PRN) prescriptions are usually taken prior to drinking or when the patient is experiencing significant cravings.

**Start:** 25mg OD for 3-4 days

**Titrate:** to 50mg OD, if needed

A slower titration may be indicated if intolerable GI symptoms or headache occur during initiation.

Limited evidence suggests a higher dose of naltrexone may be safe, with safety and tolerability demonstrated at an increased dosage of 100–150mg/day.<sup>1008,1009</sup> Dose may be increased to a maximum of 150mg per day if liver enzymes are within normal range and patient is continuing to experience cravings at 50mg per day. Note that the product monograph recommends a dose of 50mg/day to treat alcohol use disorder.

Motivation and treatment readiness may be particularly important factors for adherence, as acamprosate must be administered at a dosage of nearly 2g split into 3 doses per day due to its low bioavailability

Start at maintenance dosage:

2 x 333mg tablets TID

*\*Note: Safety and efficacy has not been fully established in these patient populations. Careful assessment of benefits and risks, fully informed patient consent, and more frequent monitoring is advised.*

## A5.2 Alternative Pharmacotherapies

Table 21.

Topiramate <sup>625</sup>	
<b>Contraindications</b>	<ol style="list-style-type: none"> <li>1. Topiramate hypersensitivity</li> <li>2. Pregnant or planning to become pregnant</li> <li>3. Narrow angle glaucoma</li> <li>4. Nephrolithiasis</li> </ol>
<b>Cautions</b>	<ol style="list-style-type: none"> <li>1. Concomitant use of valproic acid</li> <li>2. Conditions or therapies that predispose patients to acidosis (renal disease, severe respiratory disorders, status epilepticus, diarrhea, surgery, ketogenic diets, certain drugs)</li> </ol>
<b>Side effects</b>	<ul style="list-style-type: none"> <li>• CNS-related: psychomotor slowing, difficulty concentrating, speech/language problems, somnolence, fatigue, and mood disturbance</li> <li>• Most are mild to moderate in severity and occur early in treatment.</li> <li>• Start at low dose and titrate up to a stable dose over several weeks to avoid or reduce severity of side effects</li> </ul>
<b>Coverage</b>	Consult the regional drug formulary for details.
<b>Concurrent alcohol use</b>	<ul style="list-style-type: none"> <li>• No well-described safety risk</li> <li>• No interaction with alcohol and can be initiated while a patient is still drinking</li> </ul>
<b>Safety and other considerations</b>	<ul style="list-style-type: none"> <li>• Due to risk of fetal harm, advise people of childbearing potential to use effective contraceptive</li> <li>• No safety risk with liver disease</li> <li>• Monitor for signs of hyperammonemia (unexplained vomiting, lethargy, confusion, changes in mental status, hyperthermia) and metabolic acidosis (hyperventilation, fatigue, anorexia, cardiac arrhythmias, stupor)</li> </ul>

**Sample Dosing Protocol**<sup>524,525,528,530,1010,1011</sup>

- Some individuals experience significant side effects, particularly at higher doses or with more rapid increases in dosage
- Gradual dose titration over several weeks is strongly recommended (e.g., approximately 4–8 weeks to full dose).
- The recommended initial target dose for topiramate monotherapy in adults is 100mg/day, administered in 2 divided doses, as needed and tolerated.

Week	Morning Dose	Evening Dose
Week 1	None	25mg
Weeks 2–3	25mg	25mg
Weeks 3–4	50mg	50mg

If doses above 100mg/day are required, the dosage may be increased at weekly intervals in increments of 50mg up to a maximum of 400mg/day. Increases over 100mg/day should be performed in specialist settings. Studies have demonstrated better safety and tolerability of topiramate at lower doses (50–100mg/day), with side effects increasing at higher doses. Dose and titration rate should be guided by side effects and clinical outcome. Some patients may benefit from a slower titration schedule or smaller increments in dose. Daily doses above 400mg have not been adequately studied.

Table 22.

Gabapentin <sup>626</sup>	
<b>Contraindications</b>	1. Gabapentin hypersensitivity
<b>Cautions</b>	<ol style="list-style-type: none"> <li>1. Geriatric (&gt; 65 years of age) and paediatric patients (&lt; 18 years of age)<sup>a</sup></li> <li>2. Pregnant and breastfeeding patients*</li> <li>3. Concomitant use of opioids and other CNS depressants</li> <li>4. Compromised respiratory function</li> <li>5. Neurological disease or cognitive impairment</li> <li>6. Renal impairment</li> </ol>
<b>Side effects</b>	<ul style="list-style-type: none"> <li>• Side effects include ataxia, slurred speech, and drowsiness</li> <li>• Most are mild to moderate in severity, and occur early in treatment</li> </ul>

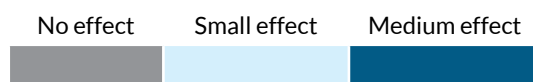
<b>Coverage</b>	Consult the regional drug formulary for details.
<b>Concurrent alcohol use</b> <sup>537,626</sup>	<ul style="list-style-type: none"> <li>• Safe to start while patients are using alcohol, but outcomes may be improved if patient has been abstinent for ≥ 3 days<sup>537</sup></li> <li>• Abstinence is recommended after starting treatment due to potential risk of combined CNS-related side effects<sup>537</sup></li> <li>• Higher than therapeutic dose and concurrent alcohol use can increase the risk of respiratory depression, profound sedation, syncope, and death. Observe patients carefully for CNS depression and adjust the dose of gabapentin as necessary</li> <li>• Completion of withdrawal management is not required prior to treatment start</li> </ul>
<b>Safety and other considerations</b> <sup>626</sup>	<ul style="list-style-type: none"> <li>• Patients with compromised respiratory function, respiratory or neurological disease, renal impairment and older adults are at higher risk of experiencing severe adverse effects on the CNS</li> <li>• Prescribe cautiously to older adults, and those with renal or cognitive impairment and provide close follow up. Do not prescribe to actively delirious patients</li> <li>• Safe to use in patients with liver disease</li> <li>• Dosage adjustment may be required with older adults and patients with renal impairment</li> <li>• Prescribers should review gabapentin’s drug–drug interactions when considering this medication as treatment for AUD</li> </ul>
<b>Sample Dosing Protocol</b> <sup>537,1012</sup>	<p>Start</p> <p>100–300mg TID</p> <p>Titrate</p> <p>If patient experiences anxiety or cravings, PRN to 1800mg max daily</p> <ul style="list-style-type: none"> <li>• If patient continues to experience insomnia, a higher HS dose may be warranted. <i>Note: This protocol applies to immediate-release (IR) tablets.</i></li> </ul> <p>Abbreviation: TID – three times per day, PRN – as needed/when necessary, HS – at bedtime</p>
<p>* <i>Note: Safety and efficacy has not been fully established in these patient populations. Careful assessment of benefit and risks, fully informed patient consent, and more frequent monitoring is advised.</i></p>	

Table 23.

Disulfiram <sup>561</sup>	
<b>Contraindications</b>	<ol style="list-style-type: none"> <li>1. Concurrent or recent use of metronidazole, alcohol or alcohol-containing preparations</li> <li>2. Alcohol intoxication</li> <li>3. Severe myocardial disease, coronary occlusion</li> <li>4. Active psychosis</li> <li>5. Hypersensitivity to disulfiram or to other thiuram (rubber) derivatives</li> </ol>
<b>Cautions</b>	<ol style="list-style-type: none"> <li>1. Pregnant and breastfeeding patients</li> <li>2. Pediatric patients</li> <li>3. Disorders including diabetes mellitus, hypothyroidism, seizure disorders, cerebral damage, chronic or acute nephritis, hepatic cirrhosis or insufficiency, abnormal EEG results, or co-occurring substance use disorders</li> </ol>
<b>Side effects</b>	<ul style="list-style-type: none"> <li>• In the absence of alcohol, most common side effects are drowsiness, skin eruptions (acne, dermatitis), fatigue, erectile dysfunction, headache, and a metallic or garlic-like aftertaste</li> <li>• A less common but serious side effect is hepatic toxicity (cholestatic or fulminant hepatitis, hepatic failure resulting in transplantation or death), which can occur in patients with and without prior history of abnormal liver function</li> </ul>
<b>Coverage</b>	<p>Consult the regional drug formulary for details.</p> <p>Note: This medication is no longer commercially sold and must be compounded at a community pharmacy. Prescribers should contact the patient's pharmacy in advance to ensure that it is available or can be accessed.</p>
<b>Concurrent alcohol use<sup>488,561</sup></b>	<ul style="list-style-type: none"> <li>• Due to severity of disulfiram–alcohol reaction, <b>patients must not consume alcohol while taking disulfiram</b></li> </ul>
<b>Safety and other considerations<sup>561</sup></b>	<ul style="list-style-type: none"> <li>• Obtain full informed consent of patient before prescribing disulfiram. Educate patients and families on side effects and risks associated with the disulfiram–alcohol reaction.</li> <li>• Patients must abstain from using alcohol for at least 12 hours before taking disulfiram.</li> <li>• The disulfiram–alcohol reaction can present as an emergency situation. Patients should carry an identification card on their person listing symptoms of disulfiram–alcohol reaction and their clinician's contact information in the event of emergencies.</li> <li>• Perform baseline and follow-up liver function tests and monitor CBC and blood chemistries due to risk of hepatotoxicity. Patients and families should be advised to immediately report early signs or symptoms of hepatitis.</li> </ul>
<b>Sample Dosing Protocol<sup>561</sup></b>	<ul style="list-style-type: none"> <li>• 250mg OD, administered as a single daily dose in morning or evening</li> <li>• Patients experiencing daytime sedation can be instructed to take their dose in the evenings. If sedation persists, dose can be reduced to 125mg</li> <li>• Patients who can still drink alcohol without experiencing a disulfiram–alcohol reaction despite good adherence (very rare) can be increased to 500mg daily</li> <li>• Do not exceed a daily dose of 500mg</li> </ul> <p>Abbreviations: OD – once daily</p>

## A5.3 Medication Selection Tool

Table 24. Comparison of AUD Pharmacotherapies



	Naltrexone	Acamprosate	Gabapentin	Topiramate
<b>Efficacy</b>				
Abstinence	Small effect	Medium effect	No effect	Medium effect
Heavy Drinking	Small effect	No effect	Medium effect	Medium effect
Craving	Small effect	No effect	No effect	No effect
<b>Contraindications (▲) and Cautions (●)</b>				
Opioid Use	▲		●	
Liver Failure / Hepatitis	▲			
Severe Kidney Impairment	●	▲	●	
Kidney Stones				▲
Narrow angle glaucoma				▲
<b>Current alcohol use</b>				
Safe to use while drinking?	✓	✓	X	✓
Pre-treatment abstinence is beneficial	✓	✓	✓	

# Appendix 6: Consultation Services

Table 25. Consultation Services by Province

Province	Resource
<b>British Columbia</b>	<p><a href="#">24/7 Addiction Medicine Clinician Support Line</a> provides telephone consultation with an addiction medicine specialist to physicians, nurse practitioners, nurses, and pharmacists on screening, assessment, treatment, and management of substance use and substance use disorders. The service is also available for any frontline care providers who are caring for individuals who use substances from Indigenous communities in BC, including Indigenous urban centres.  <b>Local calls:</b> 778-945-7619</p>
	<p><a href="#">Rapid Access to Consultative Expertise (RACE) for Addiction</a> is available for physicians and nurse practitioners M-F 0800–1700 for consultation and support.  <b>Download the RACE app:</b> <a href="http://www.raceconnect.ca/race-app">www.raceconnect.ca/race-app</a></p>
<b>Alberta</b>	<p><a href="#">Rapid Access Addiction Medicine (RAAM)</a> provides a comprehensive physician and addiction counsellor-led program managing all substance and behavioral addiction concerns M-F 0800–2100 (1700 F). Walk-in, self-referral, and professional referrals are accepted.  <b>Local calls:</b> 403-367-5000</p>
<b>Saskatchewan</b>	<p><a href="#">Rapid Access Addiction Medicine (RAAM)</a> offers walk-in services and accepts referrals from the emergency department and community care providers.</p>
<b>Manitoba</b>	<p><a href="#">Rapid Access to Addiction Medicine (RAAM) clinics</a> offers walk-in services for adults (ages 18+).  <b>Call:</b> Manitoba Addictions Helpline 1-855-662-6605  <b>RAAM on call:</b> call Health Sciences Centre (HSC) paging at 204-787-2071 and request RAAM on call</p>
	<p><a href="#">Rapid Access to Consultative Expertise (RACE) Line</a> is a telephone service available for family physicians M-F 0900–1600 for psychiatry consultation and support.  <b>Local calls:</b> 204-940-2573</p>



<p><b>Ontario</b></p>	<p>The <a href="#">Ontario eConsult program</a> is a secure web-based tool that allows physicians and nurse practitioners timely access to specialist advice for all patients, including a general addiction speciality.</p> <p><b>Sign up:</b> Use your ONEID and get same day access, visit the OTNhub <a href="#">sign up page</a> to register. For physicians without a ONEID, you can register for one through your CPSO Member Portal. If you are a nurse practitioner or need assistance getting a ONEID please email us at <a href="mailto:eConsultCOE@toh.ca">eConsultCOE@toh.ca</a>.</p> <p><a href="#">Rapid Access Addiction Medicine (RAAM) clinics</a> are low-barrier, walk-in clinics that patients can attend to get help for a substance use disorder without an appointment or formal referral. Rapid Access Addiction Medicine clinics provide time-limited medical addiction care (including pharmacotherapy, brief counselling, and referrals to community services).</p> <p>The <a href="#">Mentoring, Education and Clinical Tools for Addiction: Primary Care-Hospital Integration (META:PHI)</a> listserv is an active online community of about 1,100 doctors, nurses, counsellors, and administrators in Ontario and across Canada. It is a discussion forum for addiction-related questions, cases, articles, and policies.</p> <p><b>To access as a mailing list:</b> Send an e-mail to Laurie Smith at <a href="mailto:laurie.smith@wchospital.ca">laurie.smith@wchospital.ca</a></p> <p><b>To access as an online forum:</b> Apply for membership on the Google <a href="#">group page</a>.</p>
<p><b>Quebec</b></p>	<p>The <a href="#">CHUM Addiction Medicine Department</a> provides 24/7 support to first- and second-line nurses and physicians from every region in Quebec, whether they work in an institutional setting or in the community.</p> <p><b>Daytime:</b> 514-838-9547 (0800-1800 M-F)</p> <p><b>Evenings and weekends:</b> 514-890-8316 (1800-0800 M-F, weekends, and holidays)</p> <p><a href="#">Addiction and Homelessness Clinical and Organizational Support Team</a> provides support to health and social services professionals in Quebec with questions related to addiction and homelessness.</p> <p><b>Calls:</b> 514-863-7234 (0900-1700, M-F)</p> <p><b>Email:</b> <a href="mailto:soutien.dependance.itinerance.ccsmtl@ssss.gouv.qc.ca">soutien.dependance.itinerance.ccsmtl@ssss.gouv.qc.ca</a></p>
<p><b>Nova Scotia</b></p>	<p>The <a href="#">Addictions Medicine Consult Service (AMCS)</a> provides rapid addiction medicine consultant clinical advice and guidance to physicians, community pharmacists, and nurse practitioners.</p> <p><b>Toll-free:</b> 1-855-970-0234 (0830-1630 M-F)</p>
<p><b>Newfoundland and Labrador</b></p>	<p>The <a href="#">Building Access to Specialists through eConsultation</a> (BASE eConsult) Service is a web-based tool that allows primary care practitioners to connect with specialists. Requests will be answered within 7 days (average=2 days).</p> <p><b>Email:</b> <a href="mailto:change.management@nlchi.nl.ca">change.management@nlchi.nl.ca</a></p>

# Glossary

- 2S/LGBTQ+:** Two-Spirit, lesbian, gay, bisexual, trans, queer, and other gender and sexually diverse individuals (also see glossary entries for each respective term).
- Acamprosate:** A medication used for the treatment of AUD. Acamprosate reduces alcohol withdrawal symptoms and manages cravings by modifying responses to alcohol-related cognitive cues. It is believed to restore the imbalance between glutamate-mediated excitation and GABA-mediated inhibition of neural activity, and to reduce general neuronal hyperexcitability.
- Alcohol use disorder:** A chronic, relapsing/remitting medical condition characterized by recurrent use of alcohol and other drugs which cause significant clinical and functional impairment, exacerbated health conditions, decreased functioning and quality of life
- Benzodiazepine:** A type of CNS depressant used to treat symptoms of alcohol withdrawal.
- Bisexual:** A person who has the capacity to form enduring physical, romantic, and/or emotional attractions to those of the same gender and those of another gender. People may experience this attraction in differing ways and degrees over their lifetime.
- Carbamazepine:** An anti-convulsant medication used to treat symptoms of alcohol withdrawal.
- Clonidine:** A centrally acting alpha-2 adrenergic agonist that can suppress persistent noradrenergic symptoms (e.g., hypertension, tachycardia) associated with alcohol withdrawal.
- Continuum of AUD care:** A comprehensive system of care for the management of AUD, designed to assess and meet the evolving needs of individuals with AUD at different stages from screening and diagnosis to treatment, harm reduction, and ongoing care.
- Cultural humility:** A process undertaken through self-reflection to understand personal and systemic biases, and to develop and maintain respectful processes and relationships based on mutual trust; it requires humbly acknowledging oneself as a learner when attempting to understand another person's experience.<sup>bj</sup>

bj Definitions borrowed and lightly adapted from the [First Nations Health Authority](#).

- Cultural safety:** An outcome in which people feel safe when receiving care in an environment free from racism and discrimination. It results from respectful engagement that seeks to address power imbalances that are inherent in the health care system. It is defined by those receiving the care, not those delivering the care.
- Delirium tremens:** A serious, potentially life-threatening manifestation of alcohol withdrawal, characterized by the onset of severe confusion, disorientation, and/or hallucinations, accompanied by severe autonomic hyperactivity.
- Gabapentin:** An anti-convulsant medication used to treat symptoms of alcohol withdrawal. It is also a second-line option for ongoing AUD care.
- Gay:** The adjective used to describe people whose enduring physical, romantic, and/or emotional attractions to people of the same gender.
- Harm reduction:** Policies and programs that aim to minimize immediate health, social, and economic harms associated with the use of psychoactive substances, without necessarily requiring a decrease in substance use or a goal of abstinence.
- Health care provider:** May refer to doctors, nurse practitioners, registered nurses, registered psychiatric nurses, licensed practical nurses, and pharmacists.
- High-risk drinking:** A pattern of alcohol use associated with the development of negative physical and/or mental health consequences. Adverse social consequences are common. High-risk alcohol use is indicated by an AUDIT score  $\geq 16$  or AUDIT-C score  $\geq 8$ .
- Illicit alcohol:** See non-beverage alcohol.
- Illicit drugs:** Substances whose use is not legal or regulated.
- Lesbian:** A woman whose enduring physical, romantic, and/or emotional attraction is to other women. Some individuals fitting this description may prefer to identify as gay (adj.) or as a gay woman.<sup>bk</sup>

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bk Definitions borrowed and lightly adapted from [GLAAD Media Reference Guide](#)

- Managed alcohol program (MAP):** A harm reduction strategy used to minimize the personal harm and adverse societal effects of severe AUD, particularly as experienced by individuals who may be homeless or unstably housed. Typically, a MAP will dispense small doses of alcohol to clients at regular intervals, as a means of both regulating alcohol intake and reducing unsafe consumption of non-beverage alcohol.
- Medical management:** Medically focused, unstructured, informal counselling provided by the treating clinician in conjunction with pharmacological treatment. Medical management includes but is not limited to, performing health and wellness checks, providing support and advice, assessing motivation and identifying barriers to change, creating a treatment plan, fostering medication adherence, optimizing dosing, supporting treatment adherence and relapse prevention, and providing referrals to appropriate health and social services.
- Multigenerational trauma:** The transmission of historical oppression and unresolved trauma from caregivers to children. May also be used to describe the emotional effects, adaptations, and coping patterns developed when living with a trauma survivor.
- Mutual-support/peer-support programs:** Support that is provided through a network of peers through meetings, open discussions of personal experiences and barriers to asking for help, sponsorship, peer-based 12-step programs, and other tools of recovery. Examples include Alcoholics Anonymous, Narcotics Anonymous, SMART Recovery, and LifeRing Secular Recovery.
- Naltrexone:** A long-acting opioid antagonist medication that prevents receptors from being activated by other opioids. Naltrexone is used to treat alcohol and opioid use disorders.
- Ongoing AUD care:** A stage within the continuum of care where patients who are engaged in AUD care (and their families, if involved in care) are offered a range of ongoing evidence-based pharmacotherapies, psychosocial treatment interventions, harm reduction services, and recovery support services, as needed over time, to continue working toward meeting their long-term goals.

- Patient-centred care:** Care that takes into account the unique needs, values, and preferences of each patient, and aims to engage and empower patients as experts in their own care, including acting as the primary agent for reducing harms related to substance use, setting individualized treatment goals that are realistic and meaningful, and collaboratively selecting treatment options or interventions that will best support achieving their individual goals.
- Peer (as in peer navigator or peer support worker):** A person who shares a common lived experience (e.g., of substance use) with the client.
- People with lived and living experience:** substances are referred to people with lived experience, while those who are currently using substances are referred to as people with living experience. This terminology is intended to highlight the status of these groups as first-hand knowledge holders and stakeholders who must be consulted for decisions related to substance use care.
- Prediction of Alcohol Withdrawal Severity Scale (PAWSS):** A score-based, clinician-administered predictive tool for assessing the risk of severe withdrawal complications.
- Psychosocial supports:** Non-therapeutic social support services that aim to improve overall individual or family stability and quality of life, which may include community services, social and family services, temporary and supported housing, income-assistance programs, vocational training, life skills education, and legal services.
- Psychosocial treatment interventions:** Structured or manualized treatments delivered by a trained care provider that incorporate principles of cognitive behavioural therapy, interpersonal therapy, motivational interviewing, dialectical behaviour therapy, contingency management, structured relapse prevention, biofeedback, family and/or group counselling. Psychosocial interventions may include culturally specific approaches such as traditional healers, Elder involvement, and Indigenous healing ceremonies.
- Queer:** An adjective used by some people whose sexuality is not heterosexual. Once considered a pejorative term, queer has been reclaimed by some 2S/LGBTQ+ people to describe themselves; however, it is not a universally accepted term even within the 2S/LGBTQ+ community.<sup>3</sup>

**Recovery:** A process of change through which individuals improve their health and wellness, live a self-directed life, and strive to reach their full potential.<sup>bl</sup>

**Relapse or return to use:** May be defined differently by each person, however, a general definition would include a re-emergence of, or increase in severity of, alcohol disorder symptoms or harms related to alcohol use following a period of stability.

**Social determinants of health:** The broad range of personal, social, economic, and environmental factors that impact the health of individuals and populations.

**Stabilization:** Stabilization will be patient-specific, depending on each patient's circumstances and needs and how they change over time. Patients' DSM-5-TR diagnoses, concurrent physical and mental health disorders, and social determinants of health (e.g., poverty, homelessness) should be identified at baseline and tracked over time. Stabilization includes clinical stabilization (e.g., lack of cravings, improved sleep quality and duration, and overall wellbeing) as well as psychosocial stabilization (e.g., integrating new activities, re-connecting with family, and attaining safe housing).

**Stigma:** A set of negative attitudes and beliefs that motivate people to fear and discriminate against other people. Stigma, whether perceived or real, often fuels myths and misconceptions, and can influence choices. It can impact attitudes about seeking treatment, reactions from family and friends, behavioral health education and awareness, and the likelihood that someone will not seek or remain in treatment.

**Trans:** Trans is an umbrella term that describes a wide range of people whose gender and/or gender expression differ from their assigned sex and/or the societal and cultural expectations of their assigned sex.<sup>3</sup>

**Trauma-informed practice:** Health care and other services grounded in an understanding of trauma that integrate the following principles: trauma awareness; safety and trustworthiness; choice, collaboration, and connection; strengths-based approaches; and skill-building. Trauma-informed services prioritize safety and empowerment and avoid approaches that are confrontational.

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<sup>bl</sup> Borrowed from the Substance Abuse and Mental Health Administration's [Working Definition of Recovery](#)

- Trauma:** Trauma can be understood as an experience that overwhelms an individual's capacity to cope. Trauma can result from a series of events or one significant event. Trauma may occur in early life (e.g., child abuse, disrupted attachment, witnessing violence toward others, or neglect) or later in life (e.g., accidents, war, unexpected loss, violence, or other life events out of one's control). Trauma rarely occurs in isolation, and often directly or indirectly impacts families and communities. Trauma is rarely a single incident. Ongoing and multiple traumas can overlap or occur simultaneously. Trauma can be devastating and can interfere with a person's sense of safety, sense of self, and sense of self-efficacy. Trauma can also impact a person's ability to regulate emotions and navigate relationships. People who have experienced trauma may use substances or other behaviours to cope with feelings of shame, terror, and powerlessness.
- Two-Spirit:** A term used by some Indigenous communities on Turtle Island to describe people with diverse gender identities, gender expressions, gender roles, and sexual orientations. Two-spirit people have historically been highly respected and honored members of community for their balanced experience, knowledge, and practice.<sup>bm</sup>
- Withdrawal:** Symptoms that can occur after long-term use of a substance is reduced or stopped; these symptoms occur if tolerance to a substance has occurred and vary according to substance. Withdrawal symptoms can include heightened emotions and temporary stress, anxiety, or depression, as well as physical effects such as nausea, vomiting, muscle aches, and cramping, among others.
- Withdrawal management/detoxification:** A set of pharmacological, psychosocial, and supportive care interventions that aim to manage withdrawal symptoms that occur when an individual with a substance use disorder stops or significantly reduces the use of that substance.

bm Definition borrowed and lightly adapted from Qmunity's ["Queer Terminology from A to Q"](#)

# References

1. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008;336(7650):924-6. doi:10.1136/bmj.39489.470347.AD
2. Health Canada. Canadian Alcohol and Drugs Survey (CADS): summary of results for 2019. Health Canada. Updated December 20, 2021. Accessed October 19, 2022, <https://www.canada.ca/en/health-canada/services/canadian-alcohol-drugs-survey/2019-summary.html>
3. American Psychiatric Association (APA). Diagnostic and statistical manual of mental disorders, 5th ed. Text Revision.(DSM-5-TR). APA Publishing; 2022.
4. National Institute on Alcohol Abuse and Alcoholism. Understanding Alcohol Use Disorder. Accessed June 3, 2022, [https://www.niaaa.nih.gov/publications/brochures-and-fact-sheets/understanding-alcohol-use-disorder#:~:text=Alcohol%20use%20disorder%20\(AUD\)%20is,%2C%20occupational%2C%20or%20health%20consequences.](https://www.niaaa.nih.gov/publications/brochures-and-fact-sheets/understanding-alcohol-use-disorder#:~:text=Alcohol%20use%20disorder%20(AUD)%20is,%2C%20occupational%2C%20or%20health%20consequences.)
5. Stolle M, Sack P-M, Thomasius R. Binge drinking in childhood and adolescence: epidemiology, consequences, and interventions. *Deutsches Ärzteblatt International*. 2009;106(19):323.
6. Buchmann AF, Schmid B, Blomeyer D, et al. Impact of age at first drink on vulnerability to alcohol-related problems: testing the marker hypothesis in a prospective study of young adults. *J Psychiatr Res*. 2009;43(15):1205-1212.
7. Dawson DA, Goldstein RB, Patricia Chou S, June Ruan W, Grant BF. Age at first drink and the first incidence of adult-onset DSM-IV alcohol use disorders. *Alcoholism: Clinical and Experimental Research*. 2008;32(12):2149-2160.
8. Paradis C, Butt, P., Shield, K., Poole, N., Wells, S., Naimi, T., Sherk, A., the Low-Risk Alcohol Drinking Guidelines Scientific Expert Panels. *Canada's Guidance on Alcohol and Health: Final Report*. 2023. Accessed January 18, 2023. [https://www.ccsa.ca/sites/default/files/2023-01/Canada%27s%20Guidance%20on%20Alcohol%20and%20Health%20Final%20Report\\_1.pdf](https://www.ccsa.ca/sites/default/files/2023-01/Canada%27s%20Guidance%20on%20Alcohol%20and%20Health%20Final%20Report_1.pdf)
9. Statistics Canada. CANSIM – 82-624-X – Table 1 – Rates of selected mental or substance use disorders, lifetime and 12 month, Canada, household 15 and older, 2012. November 27, 2015. Accessed April 3, 2020. <https://www150.statcan.gc.ca/n1/pub/82-624-x/2013001/article/tbl/tbl1-eng.htm>
10. World Health Organization. World health statistics 2021: monitoring health for the SDGs, sustainable development goals. 2021. <https://apps.who.int/iris/bitstream/handle/10665/342703/9789240027053-eng.pdf?sequence=1&isAllowed=y>
11. Health Canada. *Summary of results for the Canadian Student Tobacco, Alcohol and Drugs Survey 2018-19*. 2019. <https://www.canada.ca/en/health-canada/services/canadian-student-tobacco-alcohol-drugs-survey/2018-2019-summary.html>



12. World Health Organization. *Global status report on alcohol and health – 2018 edition*. Published September 21, 2018. Accessed April 3, 2020. [http://www.who.int/substance\\_abuse/publications/global\\_alcohol\\_report/en/](http://www.who.int/substance_abuse/publications/global_alcohol_report/en/)
13. Rehm J, Gmel Sr GE, Gmel G, et al. The relationship between different dimensions of alcohol use and the burden of disease—an update. *Addiction*. 2017;112(6):968-1001.
14. Shield K, Manthey J, Rylett M, et al. National, regional, and global burdens of disease from 2000 to 2016 attributable to alcohol use: a comparative risk assessment study. *The Lancet Public Health*. 2020;5(1):e51-e61.
15. Global Burden of Disease (GBD) 2016 Alcohol Collaborators. Alcohol use and burden for 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet*. 2018;392(10152):1015-1035. doi:10.1016/S0140-6736(18)31310-2
16. Canadian Substance Use Costs and Harms Scientific Working Group. *Canadian substance use costs and harms 2015–2017*. 2020.
17. Public Health Agency of Canada. *The Chief Public Health Officer's Report on the State of Public Health in Canada 2015: Alcohol Consumption in Canada*. Public Health Agency of Canada. Published January 3, 2016. Accessed April 6, 2020. <https://www.canada.ca/content/dam/canada/health-canada/migration/healthy-canadians/publications/departement-ministere/state-public-health-alcohol-2015-etat-sante-publique-alcool/alt/state-phac-alcohol-2015-etat-aspc-alcool-eng.pdf>
18. Crane CA, Godleski SA, Przybyla SM, Schlauch RC, Testa M. The Proximal Effects of Acute Alcohol Consumption on Male-to-Female Aggression: A Meta-Analytic Review of the Experimental Literature. *Trauma Violence Abus*. 2016;17(5):520-531. doi:10.1177/1524838015584374
19. Foran HM, O'Leary KD. Alcohol and intimate partner violence: A meta-analytic review. *Clin Psychol Rev*. 2008;28(7):1222-1234. doi:10.1016/j.cpr.2008.05.001
20. Willey H, Eastwood B, Gee IL, Marsden J. Is treatment for alcohol use disorder associated with reductions in criminal offending? A national data linkage cohort study in England. *Drug Alcohol Depend*. 2016;doi:10.1016/j.drugalcdep.2016.01.020
21. Canadian Institute for Health Information. Health indicators interactive tool: Hospitalizations entirely caused by alcohol. [https://yourhealthsystem.cihi.ca/hsp/inbrief?lang=en#!/indicators/061/hospitalizations-entirely-caused-byalcohol;/mapC1;mapLevel2;trend\(C1\);/](https://yourhealthsystem.cihi.ca/hsp/inbrief?lang=en#!/indicators/061/hospitalizations-entirely-caused-byalcohol;/mapC1;mapLevel2;trend(C1);/)
22. Canadian Institute for Health Information. *Alcohol Harm in Canada: Examining Hospitalizations Entirely Caused by Alcohol and Strategies to Reduce Alcohol Harm*. Canadian Institute for Health Information; 2017. Accessed April 6, 2020. <https://www.cihi.ca/sites/default/files/document/report-alcohol-hospitalizations-en-web.pdf>
23. Mekonen T, Chan GCK, Connor J, Hall W, Hides L, Leung J. Treatment rates for alcohol use disorders: a systematic review and meta-analysis. *Addiction*. 2021;116(10):2617-2634. doi:10.1111/add.15357
24. Hasin DS, Stinson FS, Ogburn E, Grant BF. Prevalence, correlates, disability, and comorbidity of DSM-IV alcohol abuse and dependence in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry*. 2007;64(7):830-42. doi:10.1001/archpsyc.64.7.830

25. Spithoff S, Kahan M. Primary care management of alcohol use disorder and at-risk drinking. *Can Fam Physician*. 2015;61(6):515-521.
26. O'Connor EA, Perdue LA, Senger CA, et al. *Screening and Behavioral Counseling Interventions in Primary Care to Reduce Unhealthy Alcohol Use in Adolescents and Adults: Updated Systematic Review for the U.S. Preventive Services Task Force. Evidence Synthesis No. 171. AHRQ Publication No. 18-05242-EF-1*. Agency for Healthcare Research and Quality; 2018. Accessed April 6, 2020. <https://www.uspreventiveservicestaskforce.org/Home/GetFile/1/16823/unhealthy-alcohol-use-draft-evidence-review/pdf>
27. Bradley KA, Kivlahan DR. Bringing patient-centered care to patients with alcohol use disorders. *JAMA*. 2014;311(18):1861-2. doi:10.1001/jama.2014.3629
28. Spithoff S, Turner S. A systemic failure to address at-risk drinking and alcohol use disorders: the Canadian story. Editorial Material. *CMAJ*. 2015;187(7):479-480. doi:10.1503/cmaj.140849
29. Grant BF, Goldstein RB, Saha TD, et al. Epidemiology of DSM-5 Alcohol Use Disorder Results From the National Epidemiologic Survey on Alcohol and Related Conditions III. *JAMA Psychiatry*. 2015;72(8):757-766. doi:10.1001/jamapsychiatry.2015.0584
30. Alcohol Concern, Alcohol Research UK. *The hardest hit: Addressing the crisis in alcohol treatment services*. 2018. Published May 2018. Accessed May 23, 2023. <https://alcoholchange.org.uk/publication/the-hardest-hit-addressing-the-crisis-in-alcohol-treatment>
31. Roerecke M, Gual T, Rehm J. Reduction of alcohol consumption and subsequent mortality in alcohol use disorders: Systematic review and meta-analysis. *J Clin Psychiatry*. 2013;74(12):e1181-e1189.
32. Schwarzingler M, Baillot S, Yazdanpanah Y, Rehm J, Mallet V. Contribution of alcohol use disorders on the burden of chronic hepatitis C in France, 2008–2013: A nationwide retrospective cohort study. *J Hepatol*. 2017;67(3):454-461.
33. Spithoff S, Turner S, Gomes T, Martins D, Singh S. First-line medications for alcohol use disorders among public drug plan beneficiaries in Ontario. *Can Fam Physician*. 2017;63(5):e277-e283.
34. Konrad G, Leong C, Bolton J, et al. Use of pharmacotherapy for alcohol use disorder in Manitoba, Canada: a whole-population cohort study. *PLoS ONE*. 2021;16(9):e0257025.
35. Chick J. *Unhelpful prescribing in alcohol use disorder: risk and averting risk*. Oxford University Press; 2019. p. 1-4.
36. Chan P, Yomen K, Turcios J, Richman M. Prescription for antidepressant in reducing future alcohol-related readmission in patients suffering from depression and alcohol use disorder: a retrospective medical record review. *Substance Abuse Treatment, Prevention, and Policy*. 2015;10(1):1-8.
37. Lapham GT, Achtmeyer CE, Williams EC, Hawkins EJ, Kivlahan DR, Bradley KA. Increased documented brief alcohol interventions with a performance measure and electronic decision support. *Med Care*. 2012;50(2):179-87. doi:10.1097/MLR.0b013e3181e35743

38. Schuler MS, Puttaiah S, Mojtabei R, Crum RM. Perceived Barriers to Treatment for Alcohol Problems: A Latent Class Analysis. *Psychiatr Serv*. 2015;66(11):1221-8. doi:10.1176/appi.ps.201400160
39. Oliva EM, Maisel NC, Gordon AJ, Harris AH. Barriers to use of pharmacotherapy for addiction disorders and how to overcome them. *Curr Psychiatry Rep*. 2011;13(5):374-81. doi:10.1007/s11920-011-0222-2
40. Reist D, Marlatt GA, Goldner EM, et al. *Every door is the right door: a British Columbia planning framework to address problematic substance use and addiction*. British Columbia Ministry of Health Services; 2004. Accessed April 3, 2020. [https://www.health.gov.bc.ca/library/publications/year/2004/framework\\_for\\_substance\\_use\\_and\\_addiction.pdf](https://www.health.gov.bc.ca/library/publications/year/2004/framework_for_substance_use_and_addiction.pdf)
41. Graves L, Carson G, Poole N, et al. Guideline No. 405: Screening and counselling for alcohol consumption during pregnancy. *J Obstet Gynaecol Can*. 2020;42(9):1158-1173. e1.
42. Konrad G, Leong C, Bolton JM, et al. Use of pharmacotherapy for alcohol use disorder in Manitoba, Canada: A whole-population cohort study. *PLoS ONE*. 2021;16(9):e0257025. doi:10.1371/journal.pone.0257025
43. Heinrich CJ, Cummings GR. Adoption and diffusion of evidence-based addiction medications in substance abuse treatment. *Health Serv Res*. 2014;49(1):127-52. doi:10.1111/1475-6773.12093
44. Wood E, Samet JH, Volkow ND. Physician education in addiction medicine. *JAMA*. 2013;310(16):1673-4. doi:10.1001/jama.2013.280377
45. Han B, Jones CM, Einstein EB, Powell PA, Compton WM. Use of Medications for Alcohol Use Disorder in the US: Results From the 2019 National Survey on Drug Use and Health. *JAMA Psychiatry*. 2021;78(8):922-4. doi:10.1001/jamapsychiatry.2021.1271
46. Chick J. Unhelpful Prescribing in Alcohol Use Disorder: Risk and Averting Risk. *Alcohol Alcohol*. 2019;54(1):1-4. doi:10.1093/alcalc/agy090
47. Lopez E, Jeanne G, Lefort LH, et al. Characterization of benzodiazepine misuse and comorbidities in patients with alcohol use disorder. *Fundam Clin Pharmacol*. 2021;35(6):1133-1140. doi:10.1111/fcp.12678
48. Ciraulo DA, Barlow DH, Gulliver SB, et al. The effects of venlafaxine and cognitive behavioral therapy alone and combined in the treatment of co-morbid alcohol use-anxiety disorders. *Behav Res Ther*. 2013;51(11):729-35. doi:10.1016/j.brat.2013.08.003
49. Kishi T, Sevy S, Chekuri R, Correll CU. Antipsychotics for primary alcohol dependence: a systematic review and meta-analysis of placebo-controlled trials. *J Clin Psychiatry*. 2013;74(7):e642-54. doi:10.4088/JCP.12r08178
50. Friedmann PD, Rose JS, Swift R, Stout RL, Millman RP, Stein MD. Trazodone for sleep disturbance after alcohol detoxification: a double-blind, placebo-controlled trial. *Alcohol Clin Exp Res*. 2008;32(9):1652-60. doi:10.1111/j.1530-0277.2008.00742.x
51. The College of Family Physicians of Canada (2021). A practical Approach to Substance Use Disorders for the Family Physician. Available online: <https://www.cfpc.ca/CFPC/media/PDF/MIGS-2021-Addiction-Medicine-ENG-Final.pdf>.

52. Raphael D. Chapter 1: Social Determinants of Health: Key Issues and Themes. In: Raphael D, ed. *Social Determinants of Health: Canadian Perspectives*. 3rd ed. Canadian Scholars' Press Inc.; 2016:3-31.
53. Mikkonen J, Raphael D. *Social Determinants of Health: The Canadian Facts*. 2010. [http://thecanadianfacts.org/The\\_Canadian\\_Facts.pdf](http://thecanadianfacts.org/The_Canadian_Facts.pdf)
54. Tarlov AR. Chapter 5: Social determinants of health: The sociobiological translation. In: Blane D, Brunner E, Wilkinson R, eds. *Health and Social Organization: Towards a Health Policy for the 21st Century*. 1st ed. Routledge; 1996:73-93.
55. Commission on Social Determinants of Health. *Closing the gap in a generation: health equity through action on the social determinants of health. Final Report of the Commission on Social Determinants of Health*. 2008.
56. Hankivsky O, Christoffersen A. Intersectionality and the determinants of health: a Canadian perspective. *Critical Public Health*. 2008;18(3):271-283. doi:10.1080/09581590802294296
57. Galea S, Nandi A, Vlahov D. The social epidemiology of substance use. *Epidemiol Rev*. 2004;26:36-52. doi:10.1093/epirev/mxh007
58. Jones L, Bates G, McCoy E, Bellis MA. Relationship between alcohol-attributable disease and socioeconomic status, and the role of alcohol consumption in this relationship: a systematic review and meta-analysis. *BMC Public Health*. 2015;15400. doi:10.1186/s12889-015-1720-7
59. Renalds A, Smith TH, Hale PJ. A Systematic Review of Built Environment and Health. *Fam Community Health*. 2010;33(1):68-78. doi:10.1097/FCH.0b013e3181c4e2e5
60. Gilbert PA, Zemore SE. Discrimination and drinking: A systematic review of the evidence. *Soc Sci Med*. 2016;161:178-94. doi:10.1016/j.socscimed.2016.06.009
61. Mead N, Bower P. Patient-centredness: a conceptual framework and review of the empirical literature. *Soc Sci Med*. 2000;51(7):1087-110.
62. Institute of Medicine, Committee on Crossing the Quality Chasm. *Adaptation to Mental Health and Addictive Disorders. Improving the Quality of Health Care for Mental and Substance-Use Conditions*. 2006. <http://www.ncbi.nlm.nih.gov/books/NBK19830/>
63. Barrio P, Gual A. Patient-centered care interventions for the management of alcohol use disorders: a systematic review of randomized controlled trials. *Patient Prefer Adher*. 2016;10:1823-1845. doi:10.2147/ppa.s109641
64. Robinson SM. "Alcoholic" or "Person with alcohol use disorder"? Applying person-first diagnostic terminology in the clinical domain. *Subst Abus*. 2017;38(1):9-14. doi:10.1080/08897077.2016.1268239
65. Cunningham JA, Sobell LC, Chow VMC. What's in a label - the effects of substance types and labels on treatment considerations and stigma. *J Stud Alcohol*. 1993;54(6):693-699. doi:10.15288/jsa.1993.54.693
66. Kelly JF, Westerhoff CM. Does it matter how we refer to individuals with substance-related conditions? A randomized study of two commonly used terms. *Int J Drug Policy*. 2010;21(3):202-207. doi:10.1016/j.drugpo.2009.10.010

67. A PG, O'Connor KJ, Lanzkron S, et al. Do Words Matter? Stigmatizing Language and the Transmission of Bias in the Medical Record. *J Gen Intern Med.* 2018;33(5):685-691. doi:10.1007/s11606-017-4289-2
68. Luoma JB, Twohig MP, Waltz T, et al. An investigation of stigma in individuals receiving treatment for substance abuse. *Addict Behav.* 2007;32(7):1331-1346. doi:10.1016/j.addbeh.2006.09.008
69. Schomerus G, Corrigan PW, Klauer T, Kuwert P, Freyberger HJ, Lucht M. Self-stigma in alcohol dependence: Consequences for drinking-refusal self-efficacy. *Drug Alcohol Depend.* 2011;114(1):12-17. doi:10.1016/j.drugalcdep.2010.08.013
70. Glass JE, Mowbray OP, Link BG, Kristjansson SD, Bucholz KK. Alcohol stigma and persistence of alcohol and other psychiatric disorders: A modified labeling theory approach. *Drug Alcohol Depend.* 2013;133(2):685-692. doi:10.1016/j.drugalcdep.2013.08.016
71. Public Health Agency of Canada. *Communicating about substance use in compassionate, safe and non-stigmatizing ways: A Resource for Canadian Health Professional Organizations and their Membership.* 2020. <https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/healthy-living/communicating-about-substance-use-compassionate-safe-non-stigmatizing-ways-2019/guiding-rinciples-eng.pdf>
72. Grant BF, Saha TD, Ruan WJ, et al. Epidemiology of DSM-5 Drug Use Disorder: Results From the National Epidemiologic Survey on Alcohol and Related Conditions-III. *JAMA Psychiatry.* 2016;73(1):39-47. doi:10.1001/jamapsychiatry.2015.2132
73. Goldstein RB, Smith SM, Chou SP, et al. The epidemiology of DSM-5 posttraumatic stress disorder in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions-III. *Soc Psych Psych Epid.* 2016;51(8):1137-1148. doi:10.1007/s00127-016-1208-5
74. BC Centre of Excellence in Women's Health. *Trauma-Informed Practice Guide.* 2013. May. [http://bccewh.bc.ca/wp-content/uploads/2012/05/2013\\_TIP-Guide.pdf](http://bccewh.bc.ca/wp-content/uploads/2012/05/2013_TIP-Guide.pdf)
75. Public Health Agency of Canada. *Trauma and violence-informed approaches to policy and practice.* 2018. February 2. <https://www.canada.ca/en/public-health/services/publications/health-risks-safety/trauma-violence-informed-approaches-policy-practice.html>
76. Marsh TN, Coholic D, Cote-Meek S, Najavits LM. Blending Aboriginal and Western healing methods to treat intergenerational trauma with substance use disorder in Aboriginal peoples who live in northeastern Ontario, Canada. *Harm Reduct J.* 2015;12:14. doi:10.1186/s12954-015-0046-1
77. Schmidt R, Poole N, Greaves L, Hemsing N, Centre of Excellence in Women's Health. *New Terrain: Tools to Integrate Trauma and Gender Informed Responses into Substance Use Practice and Policy.* 2018. [http://bccewh.bc.ca/wp-content/uploads/2018/06/NewTerrain\\_FinalOnlinePDF.pdf](http://bccewh.bc.ca/wp-content/uploads/2018/06/NewTerrain_FinalOnlinePDF.pdf)
78. Schmidt R, Poole N, Greaves L, Hemsing N, Centre of Excellence in Women's Health. *New Terrain: Tools to Integrate Trauma and Gender Informed Responses into Substance Use Practice and Policy.* Centre of Excellence in Women's Health; 2018. Accessed April 6, 2020. [http://bccewh.bc.ca/wp-content/uploads/2018/06/NewTerrain\\_FinalOnlinePDF.pdf](http://bccewh.bc.ca/wp-content/uploads/2018/06/NewTerrain_FinalOnlinePDF.pdf)
79. Manitoba Trauma Information and Education Centre. *The Trauma-Informed Toolkit.* 2013. <https://trauma-informed.ca/recovery/resources/>

80. Substance Abuse and Mental Health Services Administration (SAMHSA), Center for Substance Abuse Treatment. *Trauma-Informed Care in Behavioral Health Services. Treatment Improvement Protocol (TIP) Series 57. HHS Publication No. (SMA) 13-4801.* SAMHSA; 2014. Accessed April 6, 2020. [https://www.integration.samhsa.gov/clinical-practice/SAMSA\\_TIP\\_Trauma.pdf](https://www.integration.samhsa.gov/clinical-practice/SAMSA_TIP_Trauma.pdf)
81. EQUIP Health Care, Research to Equip Health Care for Equity. *Trauma- and Violence-Informed Care (TVIC). A Tool for Health & Social Service Organizations and Providers.* 2018. Published March 14, 2018. Accessed April 6, 2020. <https://equiphealthcare.ca/equip/wp-content/uploads/2018/03/TVIC-BC-Mar-14-2018.pdf>
82. Farahmand P, Arshed A, Bradley MV. Systemic Racism and Substance Use Disorders. *Psychiatric annals.* 2020;50(11):494-498. doi:10.3928/00485713-20201008-01
83. Matsuzaka S, Knapp M. Anti-racism and substance use treatment: Addiction does not discriminate, but do we? *J Ethn Subst Abuse.* 2020;19(4):567-593. doi:10.1080/15332640.2018.1548323
84. Glass JE, Williams EC, Oh H. Racial/ethnic discrimination and alcohol use disorder severity among United States adults. *Drug Alcohol Depend.* 2020;216:108203. doi:10.1016/j.drugalcdep.2020.108203
85. Gilbert PA, Zemore SE. Discrimination and drinking: A systematic review of the evidence. *Social Science & Medicine.* 2016;161:178-194. doi:<https://doi.org/10.1016/j.socscimed.2016.06.009>
86. Hassen N, Lofters A, Michael S, Mall A, Pinto AD, Rackal J. Implementing Anti-Racism Interventions in Healthcare Settings: A Scoping Review. *Int J Environ Res Public Health.* 2021;18(6):2993. doi:10.3390/ijerph18062993
87. Bhatti-Sinclair K. *Anti-racist practice in social work.* Bloomsbury Publishing; 2011.
88. Matsuzaka S, Knapp M. 'Uncomfortable' is Not Enough: Integrating Anti-racism within Addiction Treatment. <https://www.basisonline.org/2020/06/integrating-antiracism-addiction-treatment.html>
89. McKenzie K, Agic B, Tuck A, Antwi M. The case for diversity: Building the case to improve mental health services for immigrant, refugee, ethno-cultural and racialized populations. *Mental Health Commission of Canada.* 2016:2016-10.
90. Puri N, Allen K, Rieb L. Treatment of alcohol use disorder among people of South Asian ancestry in Canada and the United States: A narrative review. *J Ethn Subst Abuse.* 2020;19(3):345-357. doi:10.1080/15332640.2018.1532855
91. Forman RF, Nagy PD, Center for Substance Abuse T, Bookshelf N. *Substance abuse: clinical issues in intensive outpatient treatment.* vol no. BKD 551;47;no. BKD 551;47.;no. (SMA) 06-4182.;no. (SMA) 06-4182;. U.S. Dept. of Health and Human Services, Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Treatment; 2006.
92. Gracey M, King M. Indigenous health part 1: determinants and disease patterns. *Lancet.* 2009;374(9683):65-75. doi:10.1016/S0140-6736(09)60914-4
93. King M, Smith A, Gracey M. Indigenous health part 2: the underlying causes of the health gap. *Lancet.* 2009;374(9683):76-85. doi:10.1016/S0140-6736(09)60827-8

94. Alfred GT. Colonialism and State Dependency. *Journal of Aboriginal Health*. 2009;5(2):42-60.
95. Park J, Tjepkema M, Goedhuis N, Pennock J. Avoidable mortality among First Nations adults in Canada: A cohort analysis. *Health Rep*. 2015;26(8):10-6.
96. Tjepkema M, Wilkins R, Senecal S, Guimond E, Penney C. Potential years of life lost at ages 25 to 74 among Metis and non-Status Indians, 1991 to 2001. *Health Rep*. 2011;22(1)
97. Tjepkema M, Wilkins R, Senecal S, Guimond E, Penney C. Mortality of urban Aboriginal adults in Canada, 1991-2001. *Chronic Dis Can*. 2010;31(1):4-21.
98. Ryan CJ, Cooke M, Leatherdale ST. Factors associated with heavy drinking among off-reserve First Nations and Metis youth and adults: Evidence from the 2012 Canadian Aboriginal Peoples Survey. *Prev Med*. 2016;87:95-102. doi:10.1016/j.ypmed.2016.02.008
99. The Indigenous Physicians Association of Canada (IPAC), the Royal College of Physicians and Surgeons of Canada (RCPSC). *Promoting Culturally Safe Care for First Nations, Inuit and Métis Patients; A Core Curriculum for Residents and Physicians*. 2009. [http://www.ipac-amac.ca/wp-content/uploads/2018/08/21118\\_RCPSC\\_CoreCurriculum\\_Binder.pdf](http://www.ipac-amac.ca/wp-content/uploads/2018/08/21118_RCPSC_CoreCurriculum_Binder.pdf)
100. Aboriginal Nurses Association of Canada (ANAC). *Cultural Competence & Cultural Safety in First Nations, Inuit, and Metis Nursing Education: An Integrated Review of the Literature*. 2009. <https://casn.ca/wp-content/uploads/2014/12/FINALReviewofLiterature.pdf>
101. Ward C, Branch C, Fridkin A. What is Indigenous Cultural Safety - and Why Should I Care About It? *Visions: BC's Mental Health And Substance Use Journal*. 2016;11(4):29-32.
102. Macaulay AC. Improving aboriginal health. *How can health care professionals contribute?* 2009;55(4):334-336.
103. Harm Reduction International. *What is Harm Reduction?* Accessed April 6, 2020. <https://www.hri.global/what-is-harm-reduction>
104. Logan DE, Marlatt GA. Harm Reduction Therapy: A Practice-Friendly Review of Research. *J Clin Psychol*. 2010;66(2):201-214. doi:10.1002/jclp.20669
105. Shaw GK, Waller S, Latham CJ, Dunn G, Thomson AD. The detoxification experience of alcoholic in-patients and predictors of outcome. *Alcohol Alcohol*. 1998;33(3):291-303.
106. Whitlock EP, Polen MR, Green CA, Orleans T, Klein J. Behavioral counseling interventions in primary care to reduce risky/harmful alcohol use by adults: a summary of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2004;140(7):557-68.
107. Sitharthan T, Sitharthan G, Hough MJ, Kavanagh DJ. Cue exposure in moderation drinking: A comparison with cognitive-behavior therapy. *J Consult Clin Psychol*. 1997;65(5):878-882. doi:10.1037//0022-006x.65.5.878
108. Charlet K, Heinz A. Harm reduction-a systematic review on effects of alcohol reduction on physical and mental symptoms. *Addict Biol*. 2017;22(5):1119-1159. doi:10.1111/adb.12414

109. Rahhali N, Millier A, Briquet B, et al. Modelling the consequences of a reduction in alcohol consumption among patients with alcohol dependence based on real-life observational data. *BMC Public Health*. 2015;151271. doi:10.1186/s12889-015-2606-4
110. Hasin DS, Wall M, Witkiewitz K, et al. Change in non-abstinent WHO drinking risk levels and alcohol dependence: a 3 year follow-up study in the US general population. *Lancet Psychiatry*. 2017;4(6):469-476. doi:10.1016/s2215-0366(17)30130-x
111. Witkiewitz K, Kranzler HR, Hallgren KA, et al. Drinking Risk Level Reductions Associated with Improvements in Physical Health and Quality of Life Among Individuals with Alcohol Use Disorder. *Alcohol Clin Exp Res*. 2018;42(12):2453-2465. doi:10.1111/acer.13897
112. Canadian Aboriginal AIDS Network and Interagency Coalition on AIDS and Development. *Indigenous Harm Reduction = Reducing the Harms of Colonialism*. 2019. <http://www.icad-cisd.com/pdf/Publications/Indigenous-Harm-Reduction-Policy-Brief.pdf>
113. Substance Abuse and Mental Health Services Administration (SAMHSA). *Working Definition of Recovery*. 2012. [https://store.samhsa.gov/product/SAMHSA-s-Working-Definition-of-Recovery/PEP12-RECDEF?referer=from\\_search\\_result](https://store.samhsa.gov/product/SAMHSA-s-Working-Definition-of-Recovery/PEP12-RECDEF?referer=from_search_result)
114. Mental Health Commission of Canada. *Guidelines for Recovery-Oriented Practice*. 2015. [https://www.mentalhealthcommission.ca/sites/default/files/MHCC\\_RecoveryGuidelines\\_ENG\\_0.pdf](https://www.mentalhealthcommission.ca/sites/default/files/MHCC_RecoveryGuidelines_ENG_0.pdf)
115. Lenaerts E, Mathei C, Matthys F, et al. Continuing care for patients with alcohol use disorders: A systematic review. *Drug Alcohol Depend*. 2014;135:9-21. doi:10.1016/j.drugalcdep.2013.10.030
116. Wolfe S, Kay-Lambkin F, Bowman J, Childs S. To enforce or engage: the Relationship between coercion, treatment motivation and therapeutic alliance within community-based drug and alcohol clients *Addict Behav*. 2013;38:2187-2195.
117. Rosenthal RN, Ries RK, Zweben JE. Chapter 67: Medical Management Techniques and Collaborative Care: Integrating Behavioral with Pharmacological Interventions in Addiction Treatment. In: Ries RK, Fiellin DA, Miller SC, Saitz R, eds. *The ASAM Principles of Addiction Medicine*. 5th ed. Wolters Kluwer Health; 2014:1008-1023.
118. Velleman RD, Templeton LJ, Copello AG. The role of the family in preventing and intervening with substance use and misuse: a comprehensive review of family interventions, with a focus on young people. *Drug Alcohol Rev*. 2005;24(2):93-109. doi:10.1080/09595230500167478
119. Substance Abuse and Mental Health Services Administration (SAMHSA). *Pathways to healing and recovery: perspectives from individuals with histories of alcohol and other drug problems*. SAMHSA; 2010. Accessed April 6, 2020. [https://www.samhsa.gov/sites/default/files/recovery\\_pathways\\_report.pdf](https://www.samhsa.gov/sites/default/files/recovery_pathways_report.pdf)
120. Stokes M, Schultz P, Alpaslan A. Narrating the journey of sustained recovery from substance use disorder. *Subst Abuse Treat Prev Policy*. 2018;13(1):35. doi:10.1186/s13011-018-0167-0



121. Watson J, Toner P, Day E, et al. Youth social behaviour and network therapy (Y-SBNT): adaptation of a family and social network intervention for young people who misuse alcohol and drugs - a randomised controlled feasibility trial. *Health Technol Assess*. 2017;21(15):1-260. doi:10.3310/hta21150
122. The Canadian Bar Association BC Branch. *Children and Consent to Health Care*. Published October 18, 2017. Accessed April 6, 2020. <https://www.cbabc.org/For-the-Public/Dial-A-Law/Scripts/Health-Law/422>
123. Family Mental Health Alliance, Canadian Mental Health Association, Centre for Addiction and Mental Health, Programs OFoCMHaA. *Caring together: Families as partners in the mental health and addiction system*. 2006. [https://ontario.cmha.ca/wp-content/uploads/2006/11/caring\\_together\\_2006.pdf](https://ontario.cmha.ca/wp-content/uploads/2006/11/caring_together_2006.pdf)
124. Butt P, Beirness D, Gliksman L, Paradis C, Stockwell T. *Alcohol and health in Canada: A summary of evidence and guidelines for low risk drinking*. Canadian Centre on Substance Abuse; 2011. Published November 25, 2011. Accessed April 3, 2020. <https://www.ccsa.ca/sites/default/files/2019-04/2011-Summary-of-Evidence-and-Guidelines-for-Low-Risk%20Drinking-en.pdf>
125. McNally K, Noonan LL, Cameron M, Phillips K, Baidoobonso S, Sabapathy D. Public Awareness of Low-Risk Alcohol Use Guidelines. *Health Promot Pract*. 2019;20(6):905-913.
126. Kerr WC, Stockwell T. Understanding standard drinks and drinking guidelines. *Drug Alcohol Rev*. 2012;31(2):200-5. doi:10.1111/j.1465-3362.2011.00374.x
127. Public Health Ontario. *Awareness and Knowledge of Canada's Low-Risk Drinking Guidelines*. Accessed April 6, 2020. [https://www.publichealthontario.ca/en/eRepository/Alcohol\\_Infographics\\_LRDG.pdf](https://www.publichealthontario.ca/en/eRepository/Alcohol_Infographics_LRDG.pdf)
128. Charbonneau V GA, Martel J, Urajnik D, Dénomme J, Laclé S, Lefebvre M, Malaviarachchi D, Michel I, Thistle N., *Canada's low-risk alcohol drinking guidelines among post-secondary students*. Sudbury & District Health Unit; 2014. Accessed April 7, 2020. [http://documents.cranhr.ca/pdf/LRADG\\_Final\\_Report\\_Revised\\_July\\_2015.pdf](http://documents.cranhr.ca/pdf/LRADG_Final_Report_Revised_July_2015.pdf)
129. Fox L, Population Health Assessment Surveillance and Evaluation (PHASE) Team. *Awareness of the Low-Risk Drinking Guidelines. Rapid Risk Factor Surveillance System (RRFSS) Results*. 2018. Published May 2018. Accessed April 7, 2020. [http://www.simcoemuskokakealthstats.org/docs/default-source/focus-reports/risk-factor-reports/rrfss\\_lrdg\\_2014.pdf](http://www.simcoemuskokakealthstats.org/docs/default-source/focus-reports/risk-factor-reports/rrfss_lrdg_2014.pdf)
130. Holmes J, Brown J, Meier P, Beard E, Michie S, Buykx P. Short-term effects of announcing revised lower risk national drinking guidelines on related awareness and knowledge: a trend analysis of monthly survey data in England. *BMJ Open*. 2016;6(12)e013804. doi:10.1136/bmjopen-2016-013804
131. Sprague DJ, Vinson DC. Patient perceptions of risky drinking: Knowledge of daily and weekly low-risk guidelines and standard drink sizes. *Subst Abus*. 2017;38(3):253-256. doi:10.1080/08897077.2015.1048922
132. Lovatt M, Eadie D, Meier PS, et al. Lay epidemiology and the interpretation of low-risk drinking guidelines by adults in the United Kingdom. *Addiction*. 2015;110(12):1912-1919. doi:10.1111/add.13072
133. Shield KD, Kehoe T, Taylor B, Patra J, Rehm J. Alcohol-attributable burden of disease and injury in Canada, 2004. Article. *Int J Pub Health*. 2012;57(2):391-401. doi:10.1007/s00038-011-0247-7

134. Lim SS, Vos T, Flaxman AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380(9859):2224-60. doi:10.1016/S0140-6736(12)61766-8
135. Nelson DE, Jarman DW, Rehm J, et al. Alcohol-attributable cancer deaths and years of potential life lost in the United States. *Am J Public Health*. 2013;103(4):641-648. doi:10.2105/ajph.2012.301199
136. Rehm J, Patra J, Popova S. Alcohol-attributable mortality and potential years of life lost in Canada 2001: implications for prevention and policy. *Addiction*. 2006;101(3):373-384. doi:10.1111/j.1360-0443.2005.01338.x
137. Rehm J, Mathers C, Popova S, Thavorncharoensap M, Teerawattananon Y, Patra J. Global burden of disease and injury and economic cost attributable to alcohol use and alcohol-use disorders. Research Support, Non-U.S. Gov't. *Lancet*. 2009;373(9682):2223-33. doi:10.1016/S0140-6736(09)60746-7
138. Rehm J, Baliunas D, Borges GLG, et al. The relation between different dimensions of alcohol consumption and burden of disease: an overview. Article. *Addiction*. 2010;105(5):817-843. doi:10.1111/j.1360-0443.2010.02899.x
139. Shield KD, Taylor B, Kehoe T, Patra J, Rehm J. Mortality and potential years of life lost attributable to alcohol consumption in Canada in 2005. Article. *BMC Public Health*. 2012;12:12. 91. doi:10.1186/1471-2458-12-91
140. Canadian Coalition for Seniors' Mental Health. Canadian Guidelines on Alcohol Use Disorder Among Older Adults. [https://ccsmh.ca/wp-content/uploads/2019/12/Final\\_Alcohol\\_Use\\_DisorderV6.pdf](https://ccsmh.ca/wp-content/uploads/2019/12/Final_Alcohol_Use_DisorderV6.pdf)
141. World Health Organization. Global information system on alcohol and health. <https://www.who.int/data/gho/data/themes/global-information-system-on-alcohol-and-health>
142. Statistics Canada. Table 13-10-0096-01 Health characteristics, annual estimates. 2022;doi:<https://doi.org/10.25318/1310009601-eng>
143. Rehm J, Anderson P, Manthey J, et al. Alcohol Use Disorders in Primary Health Care: What Do We Know and Where Do We Go? *Alcohol Alcohol*. 2016;51(4):422-427. doi:10.1093/alcalc/agg127
144. Jonas DE, Garbutt JC, Amick HR, et al. Behavioral counseling after screening for alcohol misuse in primary care: a systematic review and meta-analysis for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2012;157(9):645-54. doi:10.7326/0003-4819-157-9-201211060-00544
145. Moyer VA. Screening and behavioral counseling interventions in primary care to reduce alcohol misuse: U.S. preventive services task force recommendation statement. *Ann Intern Med*. 2013;159(3):210-8. doi:10.7326/0003-4819-159-3-201308060-00652
146. Curry SJ, Krist AH, Owens DK, et al. Screening and Behavioral Counseling Interventions to Reduce Unhealthy Alcohol Use in Adolescents and Adults US Preventive Services Task Force Recommendation Statement. *JAMA*. 2018;320(18):1899-1909. doi:10.1001/jama.2018.16789

147. Reinert DF, Allen JP. The alcohol use disorders identification test: an update of research findings. *Alcohol Clin Exp Res.* 2007;31(2):185-99. doi:10.1111/j.1530-0277.2006.00295.x
148. Mitchell AJ, Bird V, Rizzo M, Hussain S, Meader N. Accuracy of one or two simple questions to identify alcohol-use disorder in primary care: a meta-analysis. *Br J Gen Pract.* 2014;64(624):e408-18. doi:10.3399/bjgp14X680497
149. Bush K, Kivlahan DR, McDonell MB, Fihn SD, Bradley KA. The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. Ambulatory Care Quality Improvement Project (ACQUIP). Alcohol Use Disorders Identification Test. *Arch Intern Med.* 1998;158(16):1789-95.
150. Feldstein SW, Miller WR. Does subtle screening for substance abuse work? A review of the Substance Abuse Subtle Screening Inventory (SASSI). *Addiction.* 2007;102(1):41-50.
151. Mulvaney-Day N, Marshall T, Piscopo KD, et al. Screening for Behavioral Health Conditions in Primary Care Settings: A Systematic Review of the Literature. *J Gen Intern Med.* 2018;33(3):335-346. doi:10.1007/s11606-017-4181-0
152. Erol A, Karpyak VM. Sex and gender-related differences in alcohol use and its consequences: Contemporary knowledge and future research considerations. *Drug Alcohol Depend.* 2015;156:1-13. doi:10.1016/j.drugalcdep.2015.08.023
153. O'Connor EA, Perdue LA, Senger CA, et al. Screening and Behavioral Counseling Interventions to Reduce Unhealthy Alcohol Use in Adolescents and Adults: An Updated Systematic Review for the U.S. Preventive Services Task Force. Evidence Synthesis, No. 171. AHRQ Publication No. 18-05242-EF-1. Agency for Healthcare Research and Quality; 2018.
154. Seale JP, Boltri JM, Shellenberger S, et al. Primary care validation of a single screening question for drinkers. *J Stud Alcohol.* 2006;67(5):778-84.
155. McNeely J, Cleland CM, Strauss SM, Palamar JJ, Rotrosen J, Saitz R. Validation of Self-Administered Single-Item Screening Questions (SISQs) for Unhealthy Alcohol and Drug Use in Primary Care Patients. *J Gen Intern Med.* 2015;30(12):1757-64. doi:10.1007/s11606-015-3391-6
156. Smith PC, Schmidt SM, Allensworth-Davies D, Saitz R. Primary care validation of a single-question alcohol screening test. *J Gen Intern Med.* 2009;24(7):783-8. doi:10.1007/s11606-009-0928-6
157. O'Connor EA, Perdue LA, Senger CA, et al. Screening and Behavioral Counseling Interventions to Reduce Unhealthy Alcohol Use in Adolescents and Adults: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. *JAMA.* 2018;320(18):1910-1928. doi:<https://dx.doi.org/10.1001/jama.2018.12086>
158. Public Health England. Guidance: Alcohol Use Screening Tests. Updated October 30, 2020. <https://www.gov.uk/government/publications/alcohol-use-screening-tests>
159. Goodman A, Fleming K, Markwick N, et al. "They treated me like crap and I know it was because I was Native": The healthcare experiences of Aboriginal peoples living in Vancouver's inner city. *Soc Sci Med.* 2017;178:87-94. doi:10.1016/j.socscimed.2017.01.053

160. Elliott CT, de Leeuw SN. Our aboriginal relations: When family doctors and aboriginal patients meet. *Can Fam Physician*. 2009;55(4):443-444.
161. Browne AJ. Moving beyond description: Closing the health equity gap by redressing racism impacting Indigenous populations. *Soc Sci Med*. 2017;184:23-26. doi:10.1016/j.socscimed.2017.04.045
162. Pearce LA, Homyra F, Dale LM, et al. Non-disclosure of drug use in outpatient health care settings: Findings from a prospective cohort study in Vancouver, Canada. *International Journal of Drug Policy*. 2020;84:102873. doi:<https://doi.org/10.1016/j.drugpo.2020.102873>
163. Government of Australia. Alcohol Treatment Guidelines for Indigenous Australians. Accessed June 10, 2022, [https://insight-prod.s3.ap-southeast-2.amazonaws.com/public/guidelines/1512005960\\_alc-treat-guide-indig1.pdf](https://insight-prod.s3.ap-southeast-2.amazonaws.com/public/guidelines/1512005960_alc-treat-guide-indig1.pdf)
164. Planning and Implementing Screening and Brief Intervention for Risky Alcohol Use: A Step-by-Step Guide for Tribal Communities (Centers for Disease Control and Prevention ) (2018).
165. Islam M, Oni H, Kylie Lee K, et al. Standardized alcohol screening in primary health care services targeting Aboriginal and Torres Strait Islander peoples in Australia. *Addict Sci Clin Pract*. 2018;13(5)
166. Harris SK, Louis-Jacques J, Knight JR. Screening and brief intervention for alcohol and other abuse. *Adolesc Med State Art Rev*. 2014;25(1):126-56.
167. Knight JR, Sherritt L, Harris SK, Gates EC, Chang G. Validity of brief alcohol screening tests among adolescents: a comparison of the AUDIT, POSIT, CAGE, and CRAFFT. *Alcohol Clin Exp Res*. 2003;27(1):67-73. doi:10.1097/01.alc.0000046598.59317.3a
168. Patton R, Deluca P, Kaner E, Newbury-Birch D, Phillips T, Drummond C. Alcohol Screening and Brief Intervention for Adolescents: The How, What and Where of Reducing Alcohol Consumption and Related Harm Among Young People. Article. *Alcohol Alcohol*. 2014;49(2):207-212. doi:10.1093/alcalc/agt165
169. Toner P, Bohnke JR, Andersen P, McCambridge J. Alcohol screening and assessment measures for young people: A systematic review and meta-analysis of validation studies. *Drug & Alcohol Dependence*. 2019;202:39-49. doi:<https://dx.doi.org/10.1016/j.drugalcdep.2019.01.030>
170. National Institute on Alcohol Abuse and Alcoholism (NIAAA). *Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide*. 2021. Accessed April 11, 2023. <http://pubs.niaaa.nih.gov/publications/Practitioner/YouthGuide/YouthGuide.pdf>
171. Brown JD, Wissow LS. Discussion of sensitive health topics with youth during primary care visits: relationship to youth perceptions of care. *J Adolesc Health*. 2009;44(1):48-54. doi:10.1016/j.jadohealth.2008.06.018
172. Smith G, Chung T, Martin C, Donovan J, Windle M. Youth alcohol screening workgroup I: Measuring consumption of alcohol as a screener in children and adolescents. *Alcohol Clin Exp Res*. 2010;34(s2)
173. Brown S, Donovan J, McGue M, Shulenberg J, Zucker R, Goldman M. Youth alcohol screening workgroup II: Determining optimal secondary screening questions. *Alcohol Clin Exp Res*. 2010;34(s2)

174. Chung T, Smith GT, Donovan JE, et al. Drinking frequency as a brief screen for adolescent alcohol problems. *Pediatrics*. 2012;129(2):205-12. doi:10.1542/peds.2011-1828
175. Kelly SM, Gryczynski J, Mitchell SG, Kirk A, O'Grady KE, Schwartz RP. Validity of brief screening instrument for adolescent tobacco, alcohol, and drug use. *Pediatrics*. 2014;133(5):819-26. doi:10.1542/peds.2013-2346
176. Clark DB, Martin CS, Chung T, et al. Screening for Underage Drinking and Diagnostic and Statistical Manual of Mental Disorders, 5th Edition Alcohol Use Disorder in Rural Primary Care Practice. *J Pediatr*. 2016;173:214-20. doi:10.1016/j.jpeds.2016.02.047
177. Wright TE, Terplan M, Ondersma SJ, et al. The role of screening, brief intervention, and referral to treatment in the perinatal period. *Am J Obstet Gynecol*. 2016;215(5):539-547. doi:10.1016/j.ajog.2016.06.038
178. Jacobson SW, Chiodo LM, Sokol RJ, Jacobson JL. Validity of maternal report of prenatal alcohol, cocaine, and smoking in relation to neurobehavioral outcome. *Pediatrics*. 2002;109(5):815-25.
179. Poole N, Isaac B. Apprehensions: Barriers to treatment for substance-using mothers. Vancouver, BC: British Columbia Centre of Excellence for Women's Health. 2001.
180. Nathoo, T., Poole, N., Wolfson, L., et al. Doorways to Conversation: Brief Intervention on Substance Use with Girls and Women. Vancouver, BC: Centre of Excellence for Women's Health, 2018. Accessed April 10, 2023. [https://cewh.ca/wp-content/uploads/2018/06/Doorways\\_ENGLISH\\_July-18-2018\\_online-version.pdf](https://cewh.ca/wp-content/uploads/2018/06/Doorways_ENGLISH_July-18-2018_online-version.pdf)
181. O'Connor MJ, Whaley SE. Alcohol use in pregnant low-income women. *J Stud Alcohol*. 2003;64(6):773-83.
182. Parkes T, Poole N, Salmon A, et al. Double exposure: a better practices review on alcohol interventions during pregnancy. Vancouver, BC: British Columbia Centre of Excellence for Women's Health; 2008. Accessed April 10, 2023. <https://cewh.ca/wp-content/uploads/2014/08/Double-Exposure.pdf>
183. Wilson D, Ronde S, Brascoupe S, et al. Health Professionals Working With First Nations, Inuit, and Metis Consensus Guideline. *J Obstet Gynaecol Can*. 2013;35(6):550-553. doi:10.1016/S1701-2163(15)30915-4
184. Society of Obstetricians and Gynaecologists Canada. No. 349-Substance Use in Pregnancy. *J Obstet Gynaecol Can*. 2017;39(10):922-937.
185. Carson G, Cox LV, Crane J, et al. No. 245-Alcohol Use and Pregnancy Consensus Clinical Guidelines. *J Obstet Gynaecol Can*. 2017;39(9):e220-e254. doi:10.1016/j.jogc.2017.06.005
186. Mauro P, Askari M, Han B. Gender difference in any alcohol screening and discussions with providers among older adults in the United States, 2015 to 2019. *Alcohol Clin Exp Res*. 2021;45:1812-1820.
187. Sharp L, Vacha-Haase T. Physician Attitudes Regarding Alcohol Use Screening in Older Adult Patients. *J Appl Gerontol*. 2011;30(2):226-240.
188. Alford DP, Almeida AB, Saitz R, et al. Should adults who screen negative for unhealthy substance use be rescreened annually? Meeting Abstract. *J Gen Intern Med*. 2009;24:169-170.

189. Department of Veterans Affairs (VA), Department of Defense (DoD). *VA/DoD clinical practice guideline for the management of substance use disorders*. 2021. April 7, 2020. Accessed February 21, 2023. <https://www.healthquality.va.gov/guidelines/MH/sud/VADoDSUDCPG.pdf>
190. Staudt A, Freyer-Adam J, John U, Meyer C, Baumann S. Stability of At-risk Alcohol Use Screening Results in a General Population Sample. *Alcoholism: Clinical and Experimental Research*. 2020;44(6):1312-1320. doi:<http://dx.doi.org/10.1111/acer.14340>
191. Canagasaby A, Vinson DC. Screening for hazardous or harmful drinking using one or two quantity-frequency questions. *Alcohol Alcohol*. 2005;40(3):208-13. doi:10.1093/alcalc/agh156
192. Taj N, Devera-Sales A, Vinson DC. Screening for problem drinking: does a single question work? *J Fam Practice*. 1998;46(4):328-35.
193. Williams R, Vinson DC. Validation of a single screening question for problem drinking. *J Fam Practice*. 2001;50(4):307-12.
194. Kranzler HR, Zhou H, Kember RL, et al. Genome-wide association study of alcohol consumption and use disorder in 274,424 individuals from multiple populations. *Nature communications*. 2019;10(1):1-11.
195. Hasin DS, O'Brien CP, Auriacombe M, et al. DSM-5 criteria for substance use disorders: recommendations and rationale *Am J Psychiatry*. 2014;170(8):834-851.
196. Bartoli F, Carra G, Crocamo C, Clerici M. From DSM-IV to DSM-5 alcohol use disorder: an overview of epidemiological data. *Addict Behav*. 2014;41:46-50.
197. Martin CS, Langenbucher JW, Chung T, Sher KJ. Truth or consequences in the diagnosis of substance use disorders. *Addiction*. 2014;109(11):1773-1778.
198. Wakefield JC. DSM-5, psychiatric epidemiology and the false positives problem. *Epidemiol Psychiatr Sci*. 2015;24(3):188-96. doi:10.1017/s2045796015000116
199. Wakefield JC. DSM-5 substance use disorder: how conceptual missteps weakened the foundations of the addictive disorders field. *Acta Psychiatr Scand*. 2015;132(5):327-334. doi:<https://doi.org/10.1111/acps.12446>
200. Volkow ND, Koob GF, McLellan AT. Neurobiologic Advances from the Brain Disease Model of Addiction. *N Engl J Med*. 2016;374(4):363-71. doi:10.1056/NEJMr1511480
201. Miller WR, Rollnick S. *Motivational interviewing: Helping people change*. Guilford Press; 2012.
202. Babor TF, Higgins-Biddle JC, World Health Organization (WHO), Department of Mental Health and Substance Dependence. *Brief Intervention for Hazardous and Harmful Drinking: A Manual for Use in Primary Care*. WHO Press; 2001. Accessed April 7, 2020. [http://apps.who.int/iris/bitstream/handle/10665/67210/WHO\\_MSD\\_MSB\\_01.6b.pdf](http://apps.who.int/iris/bitstream/handle/10665/67210/WHO_MSD_MSB_01.6b.pdf)
203. Whitlock EP, Orleans CT, Pender N, Allan J. Evaluating primary care behavioral counseling interventions - An evidence-based approach. *Am J Prev Med*. 2002;22(4):267-284. doi:10.1016/s0749-3797(02)00415-4

204. Agency for Healthcare Research and Quality (AHRQ). *Five Major Steps to Intervention (The "5 A's")*. AHRQ. Published December 2012. Accessed April 7, 2020. <http://www.ahrq.gov/professionals/clinicians-providers/guidelines-recommendations/tobacco/5steps.html>
205. O'Donnell A, Anderson P, Newbury-Birch D, et al. The impact of brief alcohol interventions in primary healthcare: a systematic review of reviews. *Alcohol Alcohol*. 2014;49(1):66-78. doi:10.1093/alcalc/agt170
206. Bogg T, Marshbanks MR, Doherty HK, Vo PT. Testing a brief motivational-interviewing educational commitment module for at-risk college drinkers: A randomized trial. *Addict Behav*. 2019;90:151-157. doi:<https://dx.doi.org/10.1016/j.addbeh.2018.10.028>
207. Martin-Perez C, Navas JF, Perales JC, et al. Brief group-delivered motivational interviewing is equally effective as brief group-delivered cognitive-behavioral therapy at reducing alcohol use in risky college drinkers. *PLoS ONE*. 2019;14(12):e0226271. doi:<http://dx.doi.org/10.1371/journal.pone.0226271>
208. Hennessy EA, Tanner-Smith EE, Mavridis D, Grant SP. Comparative Effectiveness of Brief Alcohol Interventions for College Students: Results from a Network Meta-Analysis. *Prev Sci*. 2019;20(5):715-740. doi:<https://dx.doi.org/10.1007/s11121-018-0960-z>
209. Kaner EFS, Beyer FR, Muirhead C, et al. Effectiveness of brief alcohol interventions in primary care populations. *The Cochrane database of systematic reviews*. 2018;(2)Cd004148. doi:10.1002/14651858.CD004148.pub4
210. Bien TH, Miller WR, Tonigan JS. Brief interventions for alcohol problems: a review. *Addiction*. 1993;88(3):315-35.
211. Wilk AI, Jensen NM, Havighurst TC. Meta-analysis of randomized control trials addressing brief interventions in heavy alcohol drinkers. *J Gen Intern Med*. 1997;12(5):274-83.
212. Kahan M, Wilson L, Becker L. Effectiveness of physician-based interventions with problem drinkers: a review. *CMAJ*. 1995;152(6):851-859.
213. Moyer A, Finney JW, Swearingen CE, Vergun P. Brief interventions for alcohol problems: a meta-analytic review of controlled investigations in treatment-seeking and non-treatment-seeking populations. *Addiction*. 2002;97(3):279-92.
214. Frost H, Campbell P, Maxwell M, et al. Effectiveness of Motivational Interviewing on adult behaviour change in health and social care settings: A systematic review of reviews. *PLoS ONE [Electronic Resource]*. 2018;13(10):e0204890. doi:<https://dx.doi.org/10.1371/journal.pone.0204890>
215. Kaner EFS, Dickinson HO, Beyer F, et al. The effectiveness of brief alcohol interventions in primary care settings: A systematic review. *Drug Alcohol Rev*. 2009;28(3)
216. Platt L, Melendez-Torres GJ, O'Donnell A, et al. How effective are brief interventions in reducing alcohol consumption: do the setting, practitioner group and content matter? Findings from a systematic review and metaregression analysis. Review. *BMJ Open*. 2016;6(8):20. e011473. doi:10.1136/bmjopen-2016-011473
217. Ramsey AT, Satterfield JM, Gerke DR, Proctor EK. Technology-Based Alcohol Interventions in Primary Care: Systematic Review. *J Med Internet Res*. 2019;21(4):e10859. doi:<https://dx.doi.org/10.2196/10859>

218. Riper H, Hoogendoorn A, Cuijpers P, et al. Effectiveness and treatment moderators of internet interventions for adult problem drinking: An individual patient data meta-analysis of 19 randomised controlled trials. *PLoS Medicine / Public Library of Science*. 2018;15(12):e1002714. doi:<https://dx.doi.org/10.1371/journal.pmed.1002714>
219. Smedslund G, Nilsen W, Wollscheid S, Steiro A, Fang L, Larun L. Effects of Computerized Interventions on Risky Alcohol Use Among Youth: Systematic Review. *Research on Social Work Practice*. 2019;29(7):731-740. doi:10.1177/1049731518815259
220. Hai AH, Hammock K, Velasquez MM. The Efficacy of Technology-Based Interventions for Alcohol and Illicit Drug Use Among Women of Childbearing Age: A Systematic Review and Meta-Analysis. Review. *Alcoholism: Clinical and Experimental Research*. 2019;43(12):2464-2479. doi:<http://dx.doi.org/10.1111/acer.14203>
221. Carey KB, Walsh JL, Merrill JE, et al. Using e-mail boosters to maintain change after brief alcohol interventions for mandated college students: A randomized controlled trial. *Journal of Consulting & Clinical Psychology*. 2018;86(9):787-798. doi:<https://dx.doi.org/10.1037/ccp0000339>
222. Nayak MB, Kaskutas LA, Mericle AA. Randomized Trial of an Innovative Electronic Screening and Brief Intervention for Reducing Drinking Among Women of Childbearing Age. *J Addict Med*. 2019;13(6):450-459. doi:<https://dx.doi.org/10.1097/ADM.0000000000000518>
223. Grekin ER, Beatty JR, McGoron L, et al. Testing the efficacy of motivational strategies, empathic reflections, and lifelike features in a computerized intervention for alcohol use: A factorial trial. *Psychology of Addictive Behaviors*. 2019;33(6):511-519. doi:<https://dx.doi.org/10.1037/adb0000502>
224. Knight JR, Sherritt L, Gibson EB, et al. Effect of Computer-Based Substance Use Screening and Brief Behavioral Counseling vs Usual Care for Youths in Pediatric Primary Care: A Pilot Randomized Clinical Trial. *JAMA Network Open*. 2019;2(6):e196258. doi:<https://dx.doi.org/10.1001/jamanetworkopen.2019.6258>
225. Sharpe S, Kool B, Whittaker R, et al. Effect of a text message intervention on alcohol-related harms and behaviours: secondary outcomes of a randomised controlled trial. *BMC Research Notes*. 2019;12(1):267. doi:<https://dx.doi.org/10.1186/s13104-019-4308-y>
226. Guillemont J, Cogordan C, Nalpas B, Nguyen-Thanh V, Richard JB, Arwidson P. Effectiveness of a web-based intervention to reduce alcohol consumption among French hazardous drinkers: a randomized controlled trial. *Health Educ Res*. 2017;32(4):332-342. doi:<https://dx.doi.org/10.1093/her/cyx052>
227. Acuff SF, Voss AT, Dennhardt AA, Borsari B, Martens MP, Murphy JG. Brief Motivational Interventions Are Associated with Reductions in Alcohol-Induced Blackouts Among Heavy Drinking College Students. *Alcoholism: Clinical & Experimental Research*. 2019;43(5):988-996. doi:<https://dx.doi.org/10.1111/acer.14019>
228. Baumann S, Staudt A, Freyer-Adam J, Bischof G, Meyer C, John U. Effects of a brief alcohol intervention addressing the full spectrum of drinking in an adult general population sample: a randomized controlled trial. *Addiction*. 2021;116(8):2056-2066.
229. Steele DW, Becker SJ, Danko KJ, et al. Brief Behavioral Interventions for Substance Use in Adolescents: A Meta-analysis. *Pediatrics*. 2020;144:14. doi:<https://dx.doi.org/10.1542/peds.2020-0351>



230. Newton AS, Mushquash C, Krank M, et al. When and How Do Brief Alcohol Interventions in Primary Care Reduce Alcohol Use and Alcohol-Related Consequences among Adolescents? *J Pediatr*. 2018;197:221-232.e2. doi:10.1016/j.jpeds.2018.02.002
231. Mitchell SG, Gryczynski J, Schwartz RP, et al. Adolescent SBIRT implementation: Generalist vs. Specialist models of service delivery in primary care. *J Subst Abuse Treat*. 2020;111:67-72. doi:<https://dx.doi.org/10.1016/j.jsat.2020.01.007>
232. Gruenewald PJ, Johnson FW, Ponicki WR, Lascola EA. A dose-response perspective on college drinking and related problems. *Addiction*. 2010;105(2):257-69. doi:10.1111/j.1360-0443.2009.02767.x
233. Thompson KD, Stockwell T, MacDonald S. Is there a 'low-risk' drinking level for youth? The risk of acute harm as a function of quantity and frequency of drinking. *Drug and Alcohol Review*. 2012;31(2):184-193. doi:<https://doi.org/10.1111/j.1465-3362.2011.00378.x>
234. Stade BC, Bailey C, Dzendoletas D, Sgro M, Dowswell T, Bennett D. Psychological and/or educational interventions for reducing alcohol consumption in pregnant women and women planning pregnancy. *Cochrane Database Syst Rev*. 2009;(2):CD004228. doi:<https://dx.doi.org/10.1002/14651858.CD004228.pub2>
235. O'Connor MJ, Whaley SE. Brief intervention for alcohol use by pregnant women. *Am J Public Health*. 2007;97(2):252-258.
236. Parkes T, Poole N, Salmon A, Greaves L, Urquhart C. *Double exposure: a better practices review on alcohol interventions during pregnancy*. 2008. Accessed April 7, 2020. <http://bccewh.bc.ca/wp-content/uploads/2014/08/Double-Exposure.pdf>
237. Miller WR, Rollnick S. Ten things that motivational interviewing is not. *Behav Cogn Psychother*. 2009;37(2):129-40. doi:10.1017/s1352465809005128
238. Nilsen P. Brief alcohol intervention to prevent drinking during pregnancy: an overview of research findings. *Curr Opin Obstet Gynecol*. 2009;21(6):496-500. doi:10.1097/GCO.0b013e328332a74c
239. Armstrong-Moore R, Haighton C, Davinson N, Ling J. Interventions to reduce the negative effects of alcohol consumption in older adults: a systematic review. *BMC Public Health*. 2018;18(302)
240. Boumans J, van de Mheen D, Crutzen R, Dupont H, Bovens R, Rozema A. Understanding how and why alcohol interventions prevent and reduce problematic alcohol consumption among older adults: a systematic review. *Int J Environ Res Public Health*. 2022;19(3188)
241. Harris SK, Knight JR, Van Hook S, et al. Adolescent substance use screening in primary care: Validity of computer self-administered versus clinician-administered screening. Article. *Subst Abuse*. 2016;37(1):197-203. doi:10.1080/08897077.2015.1014615
242. Shimizu T, Bouchard M, Mavriplis C. Update on age-appropriate preventive measures and screening for Canadian primary care providers. *Can Fam Physician*. 2016;62(2):131-138.

243. Canadian Paediatric Society. Harm reduction: An approach to reducing risky health behaviours in adolescents. *Paediatr Child Health*. 2008;13(1):53-60.
244. Leslie KM, Canadian Paediatric Society, Adolescent Health Committee. *Position Statement – Harm reduction: An approach to reducing risky health behaviours in adolescents*. Published January 1, 2008. Updated February 28, 2018. Accessed April 7, 2020. <https://www.cps.ca/en/documents/position/harm-reduction-risky-health-behaviours>
245. National Alcohol Strategy Working Group, Alberta Alcohol and Drug Abuse Commission, Canadian Centre on Substance Abuse and Health Canada. *Reducing alcohol-related harm in Canada: towards a culture of moderation. Recommendations for a national alcohol strategy*. 2007. Accessed April 7, 2020. <https://www.ccsa.ca/sites/default/files/2019-05/ccsa-023876-2007.pdf>
246. Kokotailo PK, Abuse CoS. Alcohol use by youth and adolescents: a pediatric concern. *Pediatrics*. 2010;125(5):1078-87. doi:10.1542/peds.2010-0438
247. Williams EC, Johnson ML, Lapham GT, et al. Strategies to Implement Alcohol Screening and Brief Intervention in Primary Care Settings: A Structured Literature Review. *Psychol Addict Behav*. 2011;25(2):206-214. doi:10.1037/a0022102
248. Williams EC, Achtmeyer CE, Young JP, et al. Local Implementation of Alcohol Screening and Brief Intervention at Five Veterans Health Administration Primary Care Clinics: Perspectives of Clinical and Administrative Staff. *J Subst Abuse Treat*. 2015;60:27-35. doi:10.1016/j.jsat.2015.07.011
249. Babor TF, Higgins-Biddle JC, Dauser D, Burlinson JA, Zarkin GA, Bray J. Brief interventions for at-risk drinking: patient outcomes and cost-effectiveness in managed care organizations. *Alcohol Alcohol*. 2006;41(6):624-31. doi:10.1093/alcalc/agi078
250. Drummond C, Deluca P, Coulton S, et al. The Effectiveness of Alcohol Screening and Brief Intervention in Emergency Departments: A Multicentre Pragmatic Cluster Randomized Controlled Trial. *PLoS ONE*. 2014;9(6):e99463. doi:10.1371/journal.pone.0099463
251. Kaner E, Bland M, Cassidy P, et al. Effectiveness of screening and brief alcohol intervention in primary care (SIPS trial): pragmatic cluster randomised controlled trial. *BMJ*. 2013;346:e8501. doi:10.1136/bmj.e8501
252. Newbury-Birch D, Coulton S, Bland M, et al. Alcohol screening and brief interventions for offenders in the probation setting (SIPS Trial): a pragmatic multicentre cluster randomized controlled trial. *Alcohol Alcohol*. 2014;49(5):540-8. doi:10.1093/alcalc/agu046
253. Keurhorst M, van de Glind I, do Amaral-Sabadini MB, et al. Implementation strategies to enhance management of heavy alcohol consumption in primary health care: a meta-analysis. Review. *Addiction*. 2015;110(12):1877-1900. doi:10.1111/add.13088
254. Bradley KA, Williams EC, Achtmeyer CE, Volpp B, Collins BJ, Kivlahan DR. Implementation of evidence-based alcohol screening in the Veterans Health Administration. *Am J Manag Care*. 2006;12(10):597-606.
255. Hargraves D, White C, Frederick R, et al. Implementing SBIRT (Screening, Brief Intervention and Referral to Treatment) in primary care: lessons learned from a multi-practice evaluation portfolio. *Public Health Rev*. 2017;38Unsp 31. doi:10.1186/s40985-017-0077-0

256. Vendetti J, Gmyrek A, Damon D, Singh M, McRee B, Del Boca F. Screening, brief intervention and referral to treatment (SBIRT): implementation barriers, facilitators and model migration. *Addiction*. 2017;112:23-33. doi:10.1111/add.13652
257. Babor TF, Del Boca F, Bray JW. Screening, Brief Intervention and Referral to Treatment: Implications of SAMHSA's SBIRT initiative for substance abuse policy and practice. *Addiction*. 2017;112:110-117. doi:10.1111/add.13675
258. Center for Substance Abuse Treatment (CSAT), Substance Abuse and Mental Health Services Administration (SAMHSA). *Detoxification and Substance Abuse Treatment. Treatment Improvement Protocol (TIP) Series, No. 45. HHS Publication No. (SMA) 15-4131*. SAMHSA; 2015. Accessed April 7, 2020. <https://store.samhsa.gov/product/TIP-45-Detoxification-and-Substance-Abuse-Treatment/SMA15-4131>
259. British Columbia Ministry of Health. Provincial Guidelines for Biopsychosocialspiritual Withdrawal Management Services. <https://www.health.gov.bc.ca/library/publications/year/2017/adult-withdrawal-management-services-guidelines-final.pdf>
260. Kampman KM, Pettinati HM, Lynch KG, et al. Initiating acamprosate within-detoxification versus post-detoxification in the treatment of alcohol dependence. *Addict Behav*. 2009;34(6-7):581-6. doi:10.1016/j.addbeh.2009.03.014
261. Jonas DE, Amick HR, Feltner C, et al. Pharmacotherapy for Adults With Alcohol Use Disorders in Outpatient Settings A Systematic Review and Meta-analysis. Review. *JAMA*. 2014;311(18):1889-1900. doi:10.1001/jama.2014.3628
262. Heinala P, Alho H, Kiianna K, Lonnqvist J, Kuoppasalmi K, Sinclair JD. Targeted use of naltrexone without prior detoxification in the treatment of alcohol dependence: A factorial double-blind, placebo-controlled trial. *J Clin Psychopharm*. 2001;21(3):287-292. doi:10.1097/00004714-200106000-00006
263. Maldonado JR, Sher Y, Ashouri JF, et al. The "Prediction of Alcohol Withdrawal Severity Scale" (PAWSS): systematic literature review and pilot study of a new scale for the prediction of complicated alcohol withdrawal syndrome. *Alcohol*. 2014;48(4):375-90. doi:10.1016/j.alcohol.2014.01.004
264. Wartenberg AA. Chapter 43: Management of Alcohol Intoxication and Withdrawal. In: Ries RK FD, Miller SC, Saitz R, ed. *The ASAM Principles of Addiction Medicine*. 5th ed. Wolters Kluwer Health; 2014:635-651.
265. McKeon A, Frye MA, Delanty N. The alcohol withdrawal syndrome. *J Neurol Neurosur Ps*. 2008;79(8):854-62. doi:10.1136/jnnp.2007.128322
266. Littleton J. Neurochemical mechanisms underlying alcohol withdrawal. *Alcohol Health Res World*. 1998;22(1):13-24.
267. Schuckit MA. Alcohol-use disorders. *Lancet*. 2009;373(9662):492-501. doi:10.1016/s0140-6736(09)60009-x
268. Goodson CM, Clark BJ, Douglas IS. Predictors of severe alcohol withdrawal syndrome: a systematic review and meta-analysis. *Alcohol Clin Exp Res*. 2014;38(10):2664-77. doi:10.1111/acer.12529
269. Schmidt KJ, Doshi MR, Holzhausen JM, Natavio A, Cadiz M, Winegardner JE. Treatment of Severe Alcohol Withdrawal. *Ann Pharmacother*. 2016;50(5):389-401. doi:<https://dx.doi.org/10.1177/1060028016629161>

270. Holbrook AM, Crowther R, Lotter A, Cheng C, King D. Diagnosis and management of acute alcohol withdrawal. *CMAJ*. 1999;160(5):675-80.
271. Long D, Long B, Koyfman A. The emergency medicine management of severe alcohol withdrawal. *Am J Emerg Med*. 2017;35(7):1005-1011. doi:<https://dx.doi.org/10.1016/j.ajem.2017.02.002>
272. Hillbom M, Pieninkeroinen I, Leone M. Seizures in alcohol-dependent patients: epidemiology, pathophysiology and management. *CNS Drugs*. 2003;17(14):1013-1030.
273. Perry EC. Inpatient Management of Acute Alcohol Withdrawal Syndrome. *CNS Drugs*. 2014;28(5):401-410. doi:10.1007/s40263-014-0163-5
274. Mirijello A, D'Angelo C, Ferrulli A, et al. Identification and management of alcohol withdrawal syndrome. *Drugs*. 2015;75(4):353-65. doi:10.1007/s40265-015-0358-1
275. DeBellis R, Smith BS, Choi S, Malloy M. Management of delirium tremens. *J Intensive Care Med*. 2005;20(3):164-73. doi:10.1177/0885066605275353
276. Awissi DK, Lebrun G, Coursin DB, Riker RR, Skrobik Y. Alcohol withdrawal and delirium tremens in the critically ill: a systematic review and commentary. *Intensive Care Med*. 2013;39(1):16-30. doi:10.1007/s00134-012-2758-y
277. Young GP, Rores C, Murphy C, Dailey RH. Intravenous phenobarbital for alcohol withdrawal and convulsions. *Ann Emerg Med*. 1987;16(8):847-50.
278. Naranjo CA, Sellers EM, Chater K, Iversen P, Roach C, Sykora K. Nonpharmacologic intervention in acute alcohol withdrawal. *Clin Pharmacol Ther*. 1983;34(2):214-219.
279. McKay A, Koranda A, Axen D. Using a Symptom-Triggered Approach to Manage Patients in Acute Alcohol Withdrawal. Article. *Medsurg Nurs*. 2004;13(1):15-31.
280. Maldonado JR, Nguyen LH, Schader EM, Brooks JO. Benzodiazepine loading versus symptom-triggered treatment of alcohol withdrawal: a prospective, randomized clinical trial. *Gen Hosp Psychiatr*. 2012;34(6):611-617. doi:<https://doi.org/10.1016/j.genhosppsy.2012.06.016>
281. Elholm B, Larsen K, Hornnes N, Zierau F, Becker U. Alcohol withdrawal syndrome: symptom-triggered versus fixed-schedule treatment in an outpatient setting. *Alcohol Alcohol*. 2011;46(3):318-323. doi:<https://dx.doi.org/10.1093/alcalc/agr020>
282. Pribek I, Kovacs I, Kadar B, et al. Evaluation of the course and treatment of alcohol withdrawal syndrome with the Clinical Institute Withdrawal Assessment for Alcohol- Revised: A systematic review-based meta-analysis. *Drug Alcohol Depend*. 2021;220(108536)
283. Sullivan JT, Sykora K, Schneiderman J, Naranjo CA, Sellers EM. Assessment of alcohol withdrawal: the revised clinical institute withdrawal assessment for alcohol scale (CIWA-Ar). *Br J Addict*. 1989;84(11):1353-1357.
284. Knight E, Lappalainen L. Clinical Institute Withdrawal Assessment for Alcohol-Revised might be an unreliable tool in the management of alcohol withdrawal. *Can Fam Physician*. 2017;63(9):691-695.

285. Gossop M, Keane F, Stewart D, Marshall EJ, Strang J. A Short Alcohol Withdrawal Scale (SAWS): development and psychometric properties. *Addict Biol.* 2002;7(1):37-43. doi:10.1080/135562101200100571
286. Elholm B, Larsen K, Hornnes N, Zierau F, Becker U. A Psychometric Validation of the Short Alcohol Withdrawal Scale (SAWS). *Alcohol Alcohol.* 2010;45(4):361-365. doi:10.1093/alcalc/agq033
287. Ballenger JC, Post RM. Kindling as a model for alcohol withdrawal syndromes. *Br J Psychiat.* 1978;133(JUL):1-14. doi:10.1192/bjp.133.1.1
288. Samokhvalov Andriy V, Irving H, Mohapatra S, Rehm J. Alcohol consumption, unprovoked seizures, and epilepsy: A systematic review and meta-analysis. *Epilepsia.* 2010;51(7):1177-1184. doi:10.1111/j.1528-1167.2009.02426.x
289. Lejoyeux M, Solomon J, Adès J. Benzodiazepine treatment for alcohol-dependent patients. *Alcohol Alcohol.* 1998;33(6):563-75.
290. Nutt D, Adinoff B, Linnoila M. Benzodiazepines in the treatment of alcoholism. *Rec Dev Alcohol.* 1989;7:283-313.
291. Maldonado JR, Sher Y, Das S, et al. Prospective Validation Study of the Prediction of Alcohol Withdrawal Severity Scale (PAWSS) in Medically Ill Inpatients: A New Scale for the Prediction of Complicated Alcohol Withdrawal Syndrome. *Alcohol Alcohol.* 2015;50(5):509-18. doi:10.1093/alcalc/agv043
292. Wood E, Albarqouni L, Tkachuk S, et al. Will this hospitalized patient develop severe alcohol withdrawal syndrome? The rational clinical examination systematic review. *JAMA.* 2018;320(8):825-833. doi:10.1001/jama.2018.10574
293. Wetterling T, Weber B, Depfenhart M, Schneider B, Junghanns K. Development of a rating scale to predict the severity of alcohol withdrawal syndrome. *Alcohol Alcohol.* 2006;41(6):611-5. doi:10.1093/alcalc/agl068
294. Wetterling T, Kanitz RD, Besters B, et al. A new rating scale for the assessment of the alcohol-withdrawal syndrome (AWS scale). *Alcohol Alcohol.* 1997;32(6):753-60.
295. Myrick H, Anton RF. Treatment of alcohol withdrawal. *Alcohol Health Res World.* 1998;22(1):38-43.
296. Fiellin DA, Reid MC, O'Connor PG. Outpatient management of patients with alcohol problems. *Ann Intern Med.* 2000;133(10):815-827.
297. Bayard M, McIntyre J, Hill KR, Woodside J. Alcohol withdrawal syndrome. Article. *Am Fam Physician.* 2004;69(6):1443-1450.
298. Hayashida M, Alterman A, McLellan T, Mann S, Maany I, O'Brien C. Is inpatient medical alcohol detoxification justified: results of a randomized, controlled study. *NIDA Rs Mg.* 1988;81:19-25.
299. Klijsma MP, Cameron ML, Burns TP, McGuigan SM. Out-patient alcohol detoxification--outcome after 2 months. *Alcohol Alcohol.* 1995;30(5):669-73.
300. Muncie HL, Yasinian Y, Oge' L. Outpatient management of alcohol withdrawal syndrome. *Am Fam Physician.* 2013;88(9):589-95.

301. Abbott PJ, Quinn D, Knox L. Ambulatory medical detoxification for alcohol. *Am J Drug Alcohol Abuse*. 1995;21(4):549-63.
302. Work Group on Substance Use Disorders, American Psychiatric Association (APA). *American Psychiatric Association Practice Guidelines – Treatment of patients with substance use disorders*. Published 2010. Accessed April 7, 2020. [https://psychiatryonline.org/pb/assets/raw/sitewide/practice\\_guidelines/guidelines/substanceuse.pdf](https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/substanceuse.pdf)
303. Whitfield CL, Thompson G, Lamb A, Spencer V, Pfeifer M, Browning Ferrando M. Detoxification of 1,024 alcoholic patients without psychoactive-drugs. *JAMA*. 1978;239(14):1409-1410. doi:10.1001/jama.239.14.1409
304. Shaw JM, Kolesar GS, Sellers EM, Kaplan HL, Sandor P. Development of optimal treatment tactics for alcohol withdrawal .1. assessment and effectiveness of supportive care. Article. *J Clin Psychopharm*. 1981;1(6):382-389.
305. Kraemer KL, Mayo-Smith MF, Calkins DR. Independent clinical correlates of severe alcohol withdrawal. *Subst Abus*. 2003;24(4):197-209. doi:10.1080/08897070309511551
306. National Institute for Health and Clinical Excellence. *Alcohol Use Disorders: Diagnosis, Assessment and Management of Harmful Drinking and Alcohol Dependence*. Updated April 7, 2020. <https://www.nice.org.uk/guidance/cg115>
307. Fairgrieve C, Fairbairn N, Samet JH, Nolan S. Nontraditional Alcohol and Opioid Agonist Treatment Interventions. *Med Clin North Am*. 2018;102(4):683-696. doi:10.1016/j.mcna.2018.02.006
308. Pauly BB, Vallance K, Wettlaufer A, et al. Community managed alcohol programs in Canada: Overview of key dimensions and implementation. *Drug Alcohol Rev*. 2018;37(Suppl 1):S132-S139. doi:10.1111/dar.12681
309. Markowitz JS, McRae AL, Sonne SC. Oral nutritional supplementation for the alcoholic patient: a brief overview. *Ann Clin Psychiatry*. 2000;12(3):153-8.
310. Martin PR, Singleton CK, Hiller-Sturmhöfel S. The role of thiamine deficiency in alcoholic brain disease. *Alcohol research & health*. 2003;27(2):134.
311. National Institute for Health and Clinical Excellence. Alcohol-use disorders: diagnosis and management of physical complications. Updated April 12, 2017. Accessed February 28, 2023, <https://www.nice.org.uk/guidance/cg100/chapter/recommendations>
312. Liu J, Wang LN. Baclofen for alcohol withdrawal. *Cochrane Database Syst Rev*. 2019;11(11):06. doi:<https://dx.doi.org/10.1002/14651858.CD008502.pub6>
313. Lyon JE, Khan RA, Gessert CE, Larson PM, Renier CM. Treating alcohol withdrawal with oral baclofen: a randomized, double-blind, placebo-controlled trial. *J Hosp Med*. 2011;6(8):469-74. doi:10.1002/jhm.928
314. Shaw GK. Detoxification: the use of benzodiazepines. *Alcohol Alcohol*. 1995;30(6):765-70.
315. Carlson RW, Kumar NN, Wong-Mckinstry E, et al. Alcohol Withdrawal Syndrome. *Crit Care Clin*. 2012;28(4):549-85. doi:10.1016/j.ccc.2012.07.004

316. Erstad BI, Cotugno CL. Management of alcohol-withdrawal. *Am J Health-Sys Ph.* 1995;52(7):697-709.
317. Kosten TR, O'Connor PG. Management of drug and alcohol withdrawal. *N Engl J Med.* 2003;348(18):1786-1795. doi:10.1056/NEJMra020617
318. Williams D, McBride AJ. The drug treatment of alcohol withdrawal symptoms: A systematic review. *Alcohol Alcohol.* 1998;33(2):103-115.
319. Mayo-Smith MF. Pharmacological management of alcohol withdrawal. A meta-analysis and evidence-based practice guideline. American Society of Addiction Medicine Working Group on Pharmacological Management of Alcohol Withdrawal. *JAMA.* 1997;278(2):144-51.
320. Holbrook AM, Crowther R, Lotter A, Cheng C, King D. Meta-analysis of benzodiazepine use in the treatment of acute alcohol withdrawal. *CMAJ.* 1999;160(5):649-55.
321. Amato L, Minozzi S, Vecchi S, Davoli M. Benzodiazepines for alcohol withdrawal. *Cochrane Database Syst Rev.* 2010;(3)Cd005063. doi:10.1002/14651858.CD005063.pub3
322. Holleck JL, Merchant N, Gunderson CG. Symptom-Triggered Therapy for Alcohol Withdrawal Syndrome: a Systematic Review and Meta-analysis of Randomized Controlled Trials. *J Gen Intern Med.* 2019;34(6):1018-1024. doi:<https://dx.doi.org/10.1007/s11606-019-04899-7>
323. Gopal R, Chennatte SS, S S. Comparing 24-hour symptom triggered therapy and fixed schedule treatment for alcohol withdrawal symptoms—A randomized control study. *Asian Journal of Psychiatry.* 2020;48doi:10.1016/j.ajp.2019.101888
324. Smith JT, Sage M, Szeto H, et al. Outcomes after implementation of a benzodiazepine-sparing alcohol withdrawal order set in an integrated health care system. *JAMA Netw Open.* 2022;5(2):e220158.
325. L.T. Armistead KAS, C.K. Larson, J. Busby-Whitehead, S.P. Ferreri. A-TAPER: A Framework for Deprescribing Medications effectively. *Research in Social and Administrative Pharmacy.* 2021;doi:10.1016/j.sapharm.2021.11.013
326. de las Cuevas C, Sanz E, de la Fuente J. Benzodiazepines: more “behavioural” addiction than dependence. *Psychopharmacology (Berl).* 2003;167(3):297-303. doi:10.1007/s00213-002-1376-8
327. Barker MJ, Greenwood KM, Jackson M, Crowe SF. Persistence of cognitive effects after withdrawal from long-term benzodiazepine use: a meta-analysis. *Arch Clin Neuropsychol.* 2004;19:437-54.
328. Barker MJ, Greenwood KM, Jackson M, Crowe SF. Cognitive effects of long-term benzodiazepine use: a meta-analysis. *CNS Drugs.* 2004;18:37-48.
329. Verdoux H, Lagnaoui R, Begaud B. Is benzodiazepine use a risk factor for cognitive decline and dementia? A literature review of epidemiological studies. *Psychol Med.* 2005;35:307-15.
330. Rapoport MJ, Lanctot KL, Streiner DL, et al. Benzodiazepine use and driving: a meta-analysis. *J Clin Psychiatry.* 2009;70:663-73.

331. Smink BE, Egberts AC, Lusthof KJ, Uges DR, de Gier JJ. The relationship between benzodiazepine use and traffic accidents: A systematic literature review. *CNS Drugs*. 2010;24:639-53.
332. Guina J, Rossetter SR, DeRhodes BJ, Nahhas RW, Welton RS. Benzodiazepines for PTSD: A Systematic Review and Meta-Analysis. *Journal of Psychiatric Practice*. 2015;21(4):281-303.
333. Tubbs AS, Fernandez FX, Ghani SB, et al. Prescription medications for insomnia are associated with suicidal thoughts and behaviors in two nationally representative samples. *J Clin Sleep Med*. 2021;17(5):1025-1030. doi:10.5664/jcsm.9096
334. Ait-Daoud N, Malcolm RJ, Johnson BA. An overview of medication for the treatment of alcohol withdrawal and alcohol dependence with an emphasis on the use of older and new anticonvulsants. *Addict Behav*. 2006;31(9):1628-1649.
335. Minozzi S, Amato L, Vecchi S, Davoli M. Anticonvulsants for alcohol withdrawal. *Cochrane Database Syst Rev*. 2010;(3)Cd005064. doi:10.1002/14651858.CD005064.pub3
336. Lai J, Kalk N, Roberts E. The effectiveness and tolerability of anti-seizure medication in alcohol withdrawal syndrome: A systematic review, meta-analysis and GRADE of the evidence. *Addiction*. 2021; epub ahead of print
337. Barrons R, Roberts N. The role of carbamazepine and oxcarbazepine in alcohol withdrawal syndrome. *J Clin Pharm Ther*. 2010;35(2):153-167. doi:10.1111/j.1365-2710.2009.01098.x
338. Kalyoncu ÖA, Beyazyürek M, Kuru L, Solukçu R, Yazman Ü. Double-blind comparative trial with carbamazepine vs diazepam treatment of alcohol withdrawal. *Eur Neuropsychopharm*. 1996;6:1-2. doi:10.1016/0924-977X(96)87301-9
339. Malcolm R, Ballenger JC, Sturgis ET, Anton R. Double-blind controlled trial comparing carbamazepine to oxazepam treatment of alcohol withdrawal. *Am J Psychiat*. 1989;146(5):617-21. doi:10.1176/ajp.146.5.617
340. Ritola E, Malinen L. A double-blind comparison of carbamazepine and clomethiazole in the treatment of alcohol withdrawal syndrome. *Acta Psychiat Scand*. 1981;64(3):254-9.
341. Lucht M, Kuehn KU, Armbruster J, et al. Alcohol withdrawal treatment in intoxicated vs non-intoxicated patients: a controlled open-label study with tiapride/carbamazepine, clomethiazole and diazepam. *Alcohol Alcohol*. 2003;38(2):168-175. doi:10.1093/alcalc/agg050
342. Stuppaeck CH, Pycha R, Miller C, Whitworth AB, Oberbauer H, Fleischhacker WW. Carbamazepine versus oxazepam in the treatment of alcohol withdrawal: a double-blind study. *Alcohol Alcohol*. 1992;27(2):153-8.
343. Malcolm R, Myrick H, Roberts J, Wang W, Anton RF, Ballenger JC. The effects of carbamazepine and lorazepam on single versus multiple previous alcohol withdrawals in an outpatient randomized trial. *J Gen Intern Med*. 2002;17(5):349-55.
344. PrTEGRETOL® (carbamazepine) Product Monograph; tablets, 200 mg; chewable tablets, 100 mg and 200 mg; controlled-release tablets, 200 mg and 400 mg; suspension, 100 mg/tsp (5 mL). Submission Control No: 213356. Novartis Pharmaceuticals Canada Inc., Dorval, Canada. Available at: [https://pdf.hres.ca/dpd\\_pm/00045114.PDF](https://pdf.hres.ca/dpd_pm/00045114.PDF).



345. Ferrell PB, Jr., McLeod HL. Carbamazepine, HLA-B\*1502 and risk of Stevens-Johnson syndrome and toxic epidermal necrolysis: US FDA recommendations. *Pharmacogenomics*. 2008;9(10):1543-6. doi:10.2217/14622416.9.10.1543
346. U.S. Food and Drug Administration. Clinical Review, Adverse Events- Carbamazepine. Accessed September 1, 2021, [https://www.accessdata.fda.gov/drugsatfda\\_docs/nda/2007/016608s098,020712s029,021710\\_ClinRev.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/nda/2007/016608s098,020712s029,021710_ClinRev.pdf)
347. Dean L. Pratt VM, Scott SA, Pirmohamed M, eds. *Carbamazepine Therapy and HLA Genotype*. National Center for Biotechnology Information; 2015. <https://www.ncbi.nlm.nih.gov/books/NBK321445/>
348. Cheng YC, Huang YC, Huang WL. Gabapentinoids for treatment of alcohol use disorder: A systematic review and meta-analysis. *Hum Psychopharmacol*. 2020:e2751. doi:<https://dx.doi.org/10.1002/hup.2751>
349. Leung J, Hall-Flavin D, Nelson S, Schmidt K, Schak K. The role of gabapentin in the management of alcohol withdrawal and dependence *Ann Pharmacother*. 2015;49(8):897-906.
350. Myrick H, Malcolm R, Randall PK, et al. A double-blind trial of gabapentin versus lorazepam in the treatment of alcohol withdrawal. *Alcohol Clin Exp Res*. 2009;33(9):1582-8. doi:10.1111/j.1530-0277.2009.00986.x
351. Stock CJ, Carpenter L, Ying J, Greene T. Gabapentin versus chlordiazepoxide for outpatient alcohol detoxification treatment. *Ann Pharmacother*. 2013;47(7-8):961-9. doi:10.1345/aph.1R751
352. Mariani JJ, Rosenthal RN, Tross S, Singh P, Anand OP. A randomized, open-label, controlled trial of gabapentin and phenobarbital in the treatment of alcohol withdrawal. *Am J Addict*. 2006;15(1):76-84. doi:10.1080/10550490500419110
353. Bonnet U, Hamzavi-Abedi R, Specka M, Wiltfang J, Lieb B, Scherbaum N. An open trial of gabapentin in acute alcohol withdrawal using an oral loading protocol. *Alcohol Alcohol*. 2010;45(2):143-145.
354. Ghosh A, Mahintamani T, Choudhury S, Sharma N, Das S. The effectiveness of non-benzodiazepine, non-barbiturate medications for alcohol withdrawal syndrome: a Rapid systematic review. *Alcohol Alcohol* 2020; epub ahead of print
355. Lum E, Gorman SK, Slavik RS. Valproic acid management of acute alcohol withdrawal. *Ann Pharmacother*. 2006;40(3):441-448. doi:10.1345/aph.1G243
356. Myrick H, Brady KT, Malcolm R. Divalproex in the treatment of alcohol withdrawal. *Am J Drug Alcohol Abuse*. 2000;26(1):155-60.
357. Longo LP, Campbell T, Hubatch S. Divalproex sodium (Depakote) for alcohol withdrawal and relapse prevention. *J Addict Dis*. 2002;21(2):55-64. doi:10.1300/J069v21n02\_05
358. Johnson BA, Swift RM, Ait-Daoud N, DiClemente CC, Javors MA, Malcolm RJ. Development of novel pharmacotherapies for the treatment of alcohol dependence: focus on antiepileptics. *Alcohol Clin Exp Res*. 2004;28(2):295-301.
359. Cushman P. Clonidine and alcohol withdrawal. *Adv Alcohol Subst Abuse*. 1987;7(1):17-28.

360. Baumgartner GR, Rowen RC. Clonidine vs chlordiazepoxide in the management of acute alcohol-withdrawal syndrome. *Arch Intern Med*. 1987;147(7):1223-1226. doi:10.1001/archinte.147.7.1223
361. Baumgartner GR, Rowen RC. Transdermal clonidine versus chlordiazepoxide in alcohol-withdrawal - a randomized, controlled clinical-trial. *Southern Med J*. 1991;84(3):312-321.
362. Muzyk AJ, Fowler JA, Norwood DK, Chilipko A. Role of alpha2-agonists in the treatment of acute alcohol withdrawal. *Ann Pharmacother*. 2011;45(5):649-657.
363. Nadkarni A, Endsley P, Bhatia U, et al. Community detoxification for alcohol dependence: A systematic review. *Drug Alcohol Rev*. 2017;36(3):389-399. doi:10.1111/dar.12440
364. Chung T, Martin CS, Armstrong TD, Labouvie EW. Prevalence of DSM-IV alcohol diagnoses and symptoms in adolescent community and clinical samples. *J Am Acad Child Adolesc Psychiatry*. 2002;41(5):546-54. doi:10.1097/00004583-200205000-00012
365. Clark DB. Pharmacotherapy for Adolescent Alcohol Use Disorder. *CNS Drugs*. 2012;26(7):559-569.
366. Laegreid L, Olegard R, Conradi N, Hagberg G, Wahlstrom J, Abrahamsson L. Association between congenital malformations and maternal consumption of benzodiazepines: a case-control study. *Dev Med Child Neurol* 1990;32:432-441.
367. Enato E, Moretti M, Koren G. The fetal safety of benzodiazepines: an updated meta-analysis. *J Obstet Gynaecol Can*. 2011;33(1):46-48. doi:10.1016/S1701-2163(16)34772-7
368. Bhat A, Hadley A. The management of alcohol withdrawal in pregnancy--case report, literature review and preliminary recommendations. *Gen Hosp Psychiatr*. 2015;37(3):273.e271-273. doi:<https://dx.doi.org/10.1016/j.genhosppsy.2015.02.001>
369. DeVido J, Bogunovic O, Weiss RD. Alcohol use disorders in pregnancy. *Harv Rev Psychiatr*. 2015;23(2):112-21. doi:10.1097/hrp.0000000000000070
370. Smith EJ, Lui S, Terplan M. Pharmacologic interventions for pregnant women enrolled in alcohol treatment. *Cochrane Database Syst Rev*. 2009;(3):CD007361. doi:<https://dx.doi.org/10.1002/14651858.CD007361.pub2>
371. World Health Organization (WHO), Guidelines Review Committee. *WHO Guidelines for the Identification and Management of Substance Use and Substance Use Disorders in Pregnancy*. 2014. Accessed April 7, 2020. [https://www.who.int/substance\\_abuse/publications/pregnancy\\_guidelines/en/](https://www.who.int/substance_abuse/publications/pregnancy_guidelines/en/)
372. Montouris G. Gabapentin exposure in human pregnancy: results from the Gabapentin Pregnancy Registry. *Epilepsy & Behavior*. 2003;4(3):310-317. doi:[https://doi.org/10.1016/S1525-5050\(03\)00110-0](https://doi.org/10.1016/S1525-5050(03)00110-0)
373. Mulkey MA, DaiWai M. Delirium tremens in the older adult. *J Neurosci Nurs*. 2020;52(6):316-321.
374. Galvin R, Brathen A, Ivashynka M, Hillbom M, Tanasescu R, Leone MA. EFNS guidelines for diagnosis, therapy and prevention of Wernicke encephalopathy *Eur J Neurol*. 2010;17(12):1408-1418.

375. Kohli M, Charilaou P, Rousseau CP, Menezes R, Sanon M. Health care utilization in geriatric patients admitted with alcohol withdrawal from 2005 to 2014. *Am J Drug Alcohol Abuse*. 2020;46(4):478-484.
376. American Society of Addiction Medicine. The ASAM Clinical Practice Guideline on Alcohol Withdrawal Management. [https://www.asam.org/docs/default-source/quality-science/the\\_asam\\_clinical\\_practice\\_guideline\\_on\\_alcohol-1.pdf?sfvrsn=ba255c2\\_2](https://www.asam.org/docs/default-source/quality-science/the_asam_clinical_practice_guideline_on_alcohol-1.pdf?sfvrsn=ba255c2_2)
377. Small J, Curran GM, Booth B. Barriers and facilitators for alcohol treatment for women: are there more or less for rural women? *J Subst Abuse Treat*. 2010;39(1):1-13.
378. Allan J, Campbell M. Improving access to hard-to-reach services: a soft entry approach to drug and alcohol services for rural Australian Aboriginal communities. *Soc Work Health Care*. 2011;50(6):443-465.
379. Stewart H, Jameson JP, Curtin L. The relationship between stigma and self-reported willingness to use mental health services among rural and urban older adults. *Psychological services*. 2015;12(2):141.
380. Franz B, Dhanani LY, Miller WC. Rural-urban differences in physician bias toward patients with opioid use disorder. *Psychiatr Serv*. 2021;72(8):874-879.
381. Field M, Di Lemma L, Christiansen P, Dickson J. Automatic Avoidance Tendencies for Alcohol Cues Predict Drinking After Detoxification Treatment in Alcohol Dependence. *Psychol Addict Behav*. 2017;31(2):171-179. doi:10.1037/adb0000232
382. Foster JH, Marshall EJ, Peters TJ. Predictors of relapse to heavy drinking in alcohol dependent subjects following alcohol detoxification - the role of quality of life measures, ethnicity, social class, cigarette and drug use. *Addict Biol*. 1998;3(3):333-343. doi:10.1080/13556219872146
383. Manning V, Staiger PK, Hall K, et al. Cognitive Bias Modification Training During Inpatient Alcohol Detoxification Reduces Early Relapse: A Randomized Controlled Trial. *Alcohol Clin Exp Res*. 2016;40(9)doi:10.1111/acer.13163
384. Mueller SE, Petitjean S, Boening J, Wiesbeck GA. The impact of self-help group attendance on relapse rates after alcohol detoxification in a controlled study. *Alcohol Alcohol*. 2007;42(2):108-112. doi:10.1093/alcal/agl122
385. Oliva F, Nibbio G, Vizzuso P, et al. Gender Differences in Anxiety and Depression before and after Alcohol Detoxification: Anxiety and Depression as Gender-Related Predictors of Relapse. *Eur Addict Res*. 2018;24(4):163-172. doi:10.1159/000490046
386. Picci RL, Oliva F, Zuffranieri M, et al. Quality of life, alcohol detoxification and relapse: Is quality of life a predictor of relapse or only a secondary outcome measure? *Quality of Life Research*. 2014;23(10):2757-2767. doi:10.1007/s11136-014-0735-3
387. Willinger U, Lenzinger E, Hornik K, et al. Anxiety as a predictor of relapse in detoxified alcohol-dependent patients. *Alcohol Alcohol*. 2002;37(6):609-612. doi:10.1093/alcal/37.6.609
388. Pincus HA, England MJ. Improving the quality of psychosocial interventions for mental and substance use disorders: a Report from the IOM. *JAMA*. 2015;213(12):1227-1228.

389. Klimas J, Fairgrieve C, Tobin H, et al. Psychosocial interventions to reduce alcohol consumption in concurrent problem alcohol and illicit drug users. Systematic Review. *Cochrane Database Syst Rev*. 2018;(12)
390. Vannier AGL, Przybyszewski EM, Shay J, et al. Psychotherapy for Alcohol Use Disorder Is Associated With Reduced Risk of Incident Alcohol-Associated Liver Disease. *Clin Gastroenterol Hepatol*. 2022;doi:<https://doi.org/10.1016/j.cgh.2022.08.001>
391. Barrio P, Gual A. Patient-centered care interventions for the management of alcohol use disorders: a systematic review of randomized controlled trials. *Patient Preference and Adherence*. 2016;10:1823-1845. doi:10.2147/ppa.s109641
392. Rollnick S, Miller WR. What is Motivational Interviewing? *Behav Cogn Psychother*. 1995;23(04):325-334. doi:doi:10.1017/S135246580001643X
393. Hogue A, Liddle HA. Family-based treatment for adolescent substance abuse: controlled trials and new horizons in services research. *J Fam Ther*. 2009;31(2):126-154. doi:10.1111/j.1467-6427.2009.00459.x
394. Copeland J, Martin G. Web-based interventions for substance use disorders: A qualitative review. *J Subst Abuse Treat*. 2004;26(2):109-116. doi:10.1016/s0740-5472(03)00165-x
395. Sinadinovic K, Wennberg P, Johansson M, Berman AH. Targeting individuals with problematic alcohol use via Web-based cognitive-behavioral self-help modules, personalized screening feedback or assessment only: a randomized controlled trial. *Eur Addict Res*. 2014;20(6):305-18. doi:10.1159/000362406
396. Keoleian V, Polcin D, Galloway GP. Text messaging for addiction: a review. *J Psychoactive Drugs*. 2015;47(2):158-176. doi:10.1080/02791072.2015.1009200
397. Kelemen A, Minarcik E, Steets C, Liang Y. Telehealth interventions for alcohol use disorder: A systematic review. *Liver Research*. 2022;6(3):146-154. doi:<https://doi.org/10.1016/j.livres.2022.08.004>
398. McHugh RK, Hearon BA, Otto MW. Cognitive behavioral therapy for substance use disorders. *Psychiat Clin N Am*. 2010;33(3):511-25. doi:10.1016/j.psc.2010.04.012
399. Magill M, Ray L, Kiluk B, et al. A meta-analysis of cognitive-behavioral therapy for alcohol or other drug use disorders: Treatment efficacy by contrast condition. *J Consult Clin Psychol*. 2019;87(12):1093-1105. doi:<http://dx.doi.org/10.1037/ccp0000447>
400. Magill M, Kiluk BD, Ray LA. Efficacy of Cognitive Behavioral Therapy for Alcohol and Other Drug Use Disorders: Is a One-Size-Fits-All Approach Appropriate? *Subst Abuse Rehabil*. 2023;14:1-11. doi:10.2147/sar.S362864
401. Tan CJ, Shufelt T, Behan E, et al. Comparative effectiveness of psychosocial interventions in adults with harmful use of alcohol: A systematic review and network meta-analysis. *Addiction*. 2023;doi:10.1111/add.16187
402. Anton RF, O'Malley SS, Ciraulo DA, et al. Combined pharmacotherapies and behavioral interventions for alcohol dependence - The COMBINE study: a randomized controlled trial. Article. *JAMA*. 2006;295(17):2003-2017. doi:10.1001/jama.295.17.2003

403. Kiluk BD, Ray LA, Walthers J, Bernstein M, Tonigan JS, Magill M. Technology-Delivered Cognitive-Behavioral Interventions for Alcohol Use: A Meta-Analysis. *Alcoholism: Clinical & Experimental Research*. 2019;43(11):2285-2295. doi:10.1111/acer.14189
404. Hadjistavropoulos HD, Mehta S, Wilhelms A, Keough MT, Sundstrom C. A systematic review of internet-delivered cognitive behavior therapy for alcohol misuse: study characteristics, program content and outcomes. *Cogn Behav Ther*. 2020;49(4):327-346. doi:<https://dx.doi.org/10.1080/16506073.2019.1663258>
405. Repetti RL, Taylor SE, Seeman TE. Risky families: Family social environments and the mental and physical health of offspring. *Review. Psychol Bull*. 2002;128(2):330-366. doi:10.1037//0033-2909.128.2.330
406. Powers MB, Vedel E, Emmelkamp PMG. Behavioral couples therapy (BCT) for alcohol and drug use disorders: a meta-analysis. *Clin Psychol Rev*. 2008;28(6)
407. Stanton MD, Shadish WR. Outcome, attrition, and family-couples treatment for drug abuse: a meta-analysis and review of the controlled, comparative studies. *Psychol Bull*. 1997;122(2):170-91.
408. Meis LA, Griffin JM, Greer N, et al. Couple and family involvement in adult mental health treatment: A systematic review. *Review. Clin Psychol Rev*. 2013;33(2):275-286. doi:10.1016/j.cpr.2012.12.003
409. Hunter-Reel D, Witkiewitz K, Zweben A. Does session attendance by a supportive significant other predict outcomes in individual treatment for alcohol use disorders? *Alcohol Clin Exp Res*. 2012;36(7):1237-43. doi:10.1111/j.1530-0277.2011.01719.x
410. Ager RD, Yoshioka MR, Adams KB. Unilateral Spouse Therapy to Reach the Treatment-Resistant Alcohol Abusing Partner: A Randomized Controlled Trial. *Research on Social Work Practice*. 2020;30(7):802-814. doi:10.1177/1049731520931171
411. McCrady BS, Flanagan JC. The Role of the Family in Alcohol Use Disorder Recovery for Adults. *Alcohol Res*. 2021;41(1):06. doi:10.35946/arc.v41.1.06
412. O'Farrell TJ, Fals-Stewart W. Alcohol abuse. *J Marital Fam Ther*. 2003;29(1):121-46. doi:10.1111/j.1752-0606.2003.tb00387.x
413. O'Farrell TJ, Clements K. Review of outcome research on marital and family therapy in treatment for alcoholism. *J Marital Fam Ther*. 2012;38(1):122-44. doi:10.1111/j.1752-0606.2011.00242.x
414. Song Y, Li D, Zhang S, et al. The Effect of Behavior Couples Therapy on Alcohol and Drug Use Disorder: a Systematic Review and Meta-Analysis. *Alcohol Alcohol*. 2023;58(1):13-22. doi:10.1093/alcalc/agac053
415. Mutschler C, Malivoire BL, Schumm JA, Monson CM. Mechanisms and moderators of behavioural couples therapy for alcohol and substance use disorders: an updated review of the literature. *Behav Cogn Psychother*. 2022:1-22. doi:10.1017/s1352465822000042
416. McCrady BS, Epstein EE, Cook S, Jensen N, Hildebrandt T. A randomized trial of individual and couple behavioral alcohol treatment for women. *J Consult Clin Psychol*. 2009;77(2):243-56. doi:10.1037/a0014686

417. Bishop SR, Lau M, Shapiro S, et al. Mindfulness: A proposed operational definition. Article. *Clin Psychol Sci Pr*. 2004;11(3):230-241. doi:10.1093/clipsy/bph077
418. Linehan MM, Dimeff LA, Reynolds SK, et al. Dialectical behavior therapy versus comprehensive validation therapy plus 12-step for the treatment of opioid dependent women meeting criteria for borderline personality disorder. *Drug Alcohol Depend*. 2002;67(1):13-26. Pii s0376-8716(02)00011-x. doi:10.1016/s0376-8716(02)00011-x
419. Chiesa A, Serretti A. Are Mindfulness-Based Interventions Effective for Substance Use Disorders? A Systematic Review of the Evidence. *Subst Use Misuse*. 2014;49(5):492-512. doi:10.3109/10826084.2013.770027
420. Li W, Howard MO, Garland EL, McGovern P, Lazar M. Mindfulness treatment for substance misuse: A systematic review and meta-analysis. *J Subst Abuse Treat*. 2017;75:62-96. doi:10.1016/j.jsat.2017.01.008
421. Sancho M, De Gracia M, Rodriguez RC, et al. Mindfulness-Based Interventions for the Treatment of Substance and Behavioral Addictions: A Systematic Review. *Front Psychiatr*. 2018;995. doi:10.3389/fpsy.2018.00095
422. Bowen S CN, Witkiewitz K, Baer R. *Mindfulness-based relapse prevention for addictive behaviors. Mindfulness-based Treatment Approaches: A Clinician's Guide*. 2nd ed. Elsevier Academic Press; 2014.
423. Grant S, Colaiaco B, Motala A, et al. Mindfulness-based Relapse Prevention for Substance Use Disorders: A Systematic Review and Meta-analysis. *J Addict Med*. 2017;11(5):386-396. doi:10.1097/adm.0000000000000338
424. Zgierska AE, Burzinski CA, Mundt MP, et al. Mindfulness-based relapse prevention for alcohol dependence: Findings from a randomized controlled trial. *J Subst Abuse Treat*. 2019;100:8-17. doi:<https://dx.doi.org/10.1016/j.jsat.2019.01.013>
425. Adhikari S, Tulachan P, Ojha SP, Chapagai M, Dhungana S, Pant SB. Comparison of Disulfiram and Naltrexone in Cases of Alcohol Dependence Syndrome. *Journal of Nepal Health Research Council*. 2020;18(1):75-81. doi:<http://dx.doi.org/10.33314/jnhrc.v18i1.1921>
426. Davis DR, Kurti AN, Skelly JM, Redner R, White TJ, Higgins ST. A review of the literature on contingency management in the treatment of substance use disorders, 2009-2014. *Prev Med*. 2016;92:36-46. doi:10.1016/j.ypmed.2016.08.008
427. Rice D, Corace K, Wolfe D, et al. Evaluating comparative effectiveness of psychosocial interventions adjunctive to opioid agonist therapy for opioid use disorder: a Systematic review with network meta-analyses. *PLoS ONE*. 2020;15(12):e0244401.
428. Oluwoye O, Leickly E, Skalisky J, et al. Serious Mental Illness in Heavy Drinkers Is Associated with Poor Treatment Outcomes in Outpatients with Co-occurring Disorders. *International Journal of Mental Health & Addiction*. 2018;16(3):672-679.
429. Benishek LA, Dugosh KL, Kirby KC, et al. Prize-based contingency management for the treatment of substance abusers: a meta-analysis. *Addiction*. 2014;109(9):1426-1436. doi:10.1111/add.12589

430. Alessi SM, Petry NM. A randomized study of cellphone technology to reinforce alcohol abstinence in the natural environment. *Addiction*. 2013;108(5):900-909. doi:<https://dx.doi.org/10.1111/add.12093>
431. Koffarnus MN, Bickel WK, Kablinger AS. Remote Alcohol Monitoring to Facilitate Incentive-Based Treatment for Alcohol Use Disorder: A Randomized Trial. *Alcoholism: Clinical & Experimental Research*. 2018;42(12):2423-2431. doi:<https://dx.doi.org/10.1111/acer.13891>
432. Rash CJ, Stitzer M, Weinstock J. Contingency Management: New Directions and Remaining Challenges for An Evidence-Based Intervention. *J Subst Abuse Treat*. 2017;72:10-18. doi:10.1016/j.jsat.2016.09.008
433. Carroll KM. Lost in translation? Moving contingency management and cognitive behavioral therapy into clinical practice. *Ann N Y Acad Sci*. 2014;1327(1):94-111. doi:10.1111/nyas.12501
434. Kirby KC, Benishek LA, Dugosh KL, Kerwin ME. Substance abuse treatment providers' beliefs and objections regarding contingency management: implications for dissemination. *Drug Alcohol Depend*. 2006;85(1):19-27. doi:10.1016/j.drugalcdep.2006.03.010
435. Fitzsimons H, Tuten M, Borsuk C, Lookatch S, Hanks L. Clinician-delivered contingency management increases engagement and attendance in drug and alcohol treatment. *Drug Alcohol Depend*. 2015;152:62-67. doi:10.1016/j.drugalcdep.2015.04.021
436. Hartzler B, Lash SJ, Roll JM. Contingency management in substance abuse treatment: A structured review of the evidence for its transportability. *Drug Alcohol Depend*. 2012;122(1-2):1-10. doi:10.1016/j.drugalcdep.2011.11.011
437. Boffo M, Zerhouni O, Gronau QF, et al. Cognitive bias modification for behaviour change in alcohol and smoking addiction: Bayesian meta-analysis of individual participant data. *Neurosci Rev*. 2019;29:52-78.
438. Woud ML, Hutschemaekers MHM, Rinck M, Becker ES. The manipulation of alcohol-related interpretation biases by means of cognitive bias modification - interpretation (CBM-I). *J Behav Ther Exp Psychiatry*. 2015;49:61-68.
439. Cristea IA, Kok RN, Cuijpers P. The effectiveness of cognitive bias modification interventions for substance addictions: a Meta-analysis. *PLoS ONE*. 2016;11(9):e0162226.
440. Wiers RW, Boffo M, Field M. What's in a trial? On the importance of distinguishing between experimental lab studies and randomized controlled trials: the Case of cognitive bias modification and alcohol use disorders. *J Stud Alcohol Drugs*. 2018;79(3):333-343.
441. Hasin DS, Grant BF. The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) Waves 1 and 2: review and summary of findings. Review. *Soc Psych Psych Epid*. 2015;50(11):1609-1640. doi:10.1007/s00127-015-1088-0
442. Roberts NP, Roberts PA, Jones N, Bisson JI. Psychological therapies for post-traumatic stress disorder and comorbid substance use disorder. *Cochrane Database Syst Rev*. 2016;4:Cd010204. doi:10.1002/14651858.CD010204.pub2

443. Pragnell A, Shoveller J, Voon P, et al. The impact of childhood emotional abuse on pain among people with chronic pain who inject drugs in Vancouver, Canada. *Pain Med.* 2020;21(4):704-713.
444. Baker AL, Thornton LK, Hiles S, Hides L, Lubman DI. Psychological interventions for alcohol misuse among people with co-occurring depression or anxiety disorders: a systematic review. *J Affect Disord.* 2012;139(3):217-29. doi:10.1016/j.jad.2011.08.004
445. Hobbs JD, Kushner MG, Lee SS, Reardon SM, Maurer EW. Meta-analysis of supplemental treatment for depressive and anxiety disorders in patients being treated for alcohol dependence. *Am J Addict.* 2011;20(4):319-329.
446. Schäfer I, Lotzin A, Hiller P, et al. A multisite randomized controlled trial of Seeking Safety vs Relapse Prevention Training for women with co-occurring posttraumatic stress disorder and substance use disorders. *European Journal of Psychotraumatology.* 2019;10(1)doi:10.1080/20008198.2019.1577092
447. Hunt GE, Siegfried N, Morley K, Sitharthan T, Cleary M. Psychosocial interventions for people with both severe mental illness and substance misuse. *Cochrane Database Syst Rev.* 2013;(10)Cd001088. doi:10.1002/14651858.CD001088.pub3
448. Finn SW, Hammarberg A, Andreasson S. Treatment for alcohol dependence in primary care compared to outpatient specialist treatment-a randomized controlled trial. *Alcohol Alcohol.* 2018;53(4):376-385. doi:<http://dx.doi.org/10.1093/alcalc/agx126>
449. Tiet QQ, Mausbach B. Treatments for patients with dual diagnosis: a review. *Alcohol Clin Exp Res.* 2007;31(4):513-536.
450. Tripodi SJ, Bender K, Litschge C, Vaughn MG. Interventions for reducing adolescent alcohol abuse: a meta-analytic review. *Arch Pediat Adol Med.* 2010;164(1):85-91.
451. Waldron HB, Turner CW. Evidence-based psychosocial treatments for adolescent substance abuse. *J Clin Child Adolesc Psychol.* 2008;37(1):238-261. doi:10.1080/15374410701820133
452. Becker SJ, Curry JF. Outpatient interventions for adolescent substance abuse: A quality of evidence review. *J Consult Clin Psych.* 2008;76(4):531-543. doi:10.1037/0022-006x.76.4.531
453. Vaughn MG, Howard MO. Adolescent substance abuse treatment: A synthesis of controlled evaluations. *Res Social Work Prac.* 2004;14(5):325-335. doi:10.1177/1049731504265834
454. Hogue A, Dauber S, Faw Stambaugh L, Cecero JJ, Liddle HA. Early therapeutic alliance and treatment outcome in individual and family therapy and adolescent behavior problems. *J Consult Clin Psychol.* 2006;74(1):121-129.
455. Schonfeld L, Dupree LW, Dickson-Fuhrmann E, et al. Cognitive-behavioral treatment of older veterans with substance abuse problems. *J Geriatr Psychiatry Neurol.* 2000;13(3):124-129.
456. Rice C, Longanagh R, Beattie M, Noel N. Age group differences in response to treatment for problematic alcohol use. *Addiction.* 1993;88(10):1369-1375.



457. Substance Abuse and Mental Health Services Administration. Treating Substance Use Disorder in Older Adults. Treatment Improvement Protocol (TIP) Series No. 26, SAMHSA Publication No. PEP20-02-01-011. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2020.
458. Schutte K, Lemke S, Moos RH, Brennan PL. *Age-sensitive psychosocial treatment for older adults with substance abuse*. Substance Use and Older People. Wiley-Blackwell; 2015.
459. Schmidt LK, Bojesen AB, Nielsen AS, Andersen K. Duration of therapy - Does it matter? A systematic review and meta-regression of the duration of psychosocial treatments for alcohol use disorder. *J Subst Abuse Treat*. 2018;84:57-67. doi:10.1016/j.jsat.2017.11.002
460. Magill M, Ray LA. Cognitive-behavioral treatment with adult alcohol and illicit drug users: A meta-analysis of randomized controlled trials. *J Stud Alcohol Drugs*. 2009;70(4):516-527.
461. Mark T, Kassed C, Vandivort-Warren R, Levit K, Kranzler H. Alcohol and opioid dependence medications: Prescription trends, overall and by physician speciality. *Drug Alcohol Depend*. 2009;99(1):345-349.
462. Williams EC, Achtmeyer CE, Young JP, et al. Barriers to and Facilitators of Alcohol Use Disorder Pharmacotherapy in Primary Care: A Qualitative Study in Five VA Clinics. *J Gen Intern Med*. 2018;33(3):258-267. doi:10.1007/s11606-017-4202-z
463. Gregory C, Chorny Y, Mcleod S, Mohindra R. First-line medication for the outpatient treatment of alcohol use disorder: a systematic review of perceived barriers. *J Addict Med*. 2021;online ahead of print
464. Spithoff S, Kahan M. Paradigm shift: Moving the management of alcohol use disorders from specialized care to primary care. *Can Fam Physician*. 2015;61(6):491-493.
465. Vannier AG, Shay JE, Fomin V, et al. Incidence and Progression of Alcohol-Associated Liver Disease After Medical Therapy for Alcohol Use Disorder. *JAMA Network Open*. 2022;5(5):e2213014-e2213014.
466. Friedmann PD, Rose JS, Swift R, Stout RL, Millman RP, Stein MD. Trazodone for sleep disturbance after alcohol detoxification: a Double-blind, placebo-controlled trial. *Alcohol Clin Exp Res*. 2008;32(9):1652-1600.
467. Lopez E, Jeanne G, Lefort LH, et al. Characterization of benzodiazapine misuse and comorbidities in patients with alcohol use disorder. *Fundam Clin Pharmacol*. 2021;00:1-8.
468. Charney DA, Heath LM, Zikos E, Palacios-Boix J, Gill KJ. Poorer drinking outcomes with citalopram treatment for alcohol dependence: a Randomized, double-blinded, placebo-controlled trial. *Alcohol Clin Exp Res*. 2015;39(9):1756-1765.
469. Gastfriend DR, Garbutt JC, Pettinati HM, Forman RF. Reduction in heavy drinking as a treatment outcome in alcohol dependence. *J Subst Abuse Treat*. 2007;33(1):71-80. doi:10.1016/j.jsat.2006.09.008
470. Finn S, Bakshi A, S A. Alcohol consumption, dependence, and treatment barriers: Perceptions among nontreatment seekers with alcohol dependence *Subst Use Misuse* 2014;49(6):762-769.

471. Hodgins DC, Leigh G, Milne R, Gerrish R. Drinking goal selection in behavioral selfmanagement treatment of chronic alcoholics. *Addict Behav.* 1997;22(2):247-255. doi:10.1016/s0306-4603(96)00013-5
472. Al-Otaiba Z, Worden BL, McCrady BS, Epstein EE. Accounting for self-selected drinking goals in the assessment of treatment outcome. *Psychol Addict Behav.* 2008;22(3):439-443. doi:10.1037/0893-164x.22.3.439
473. Berglund KJ, Svensson I, Berggren U, Balldin J, C F. Is there a need for congruent treatment goals between alcohol-dependent patients and caregivers? *Alcohol Clin Exp Res.* 2016;40(4):874-879.
474. Adamson SJ, Heather N, Morton V, Raistrick. D. Initial preference for drinking goal in the treatment of alcohol problems: II. treatment outcomes. *Alcohol Alcohol.* 2010;45(2):136-142.
475. Bujarski S, O'Malley SS, Lunny K, Ray LA. The effects of drinking goal on treatment outcome for alcoholism. *J Consult Clin Psychol.* 2013;81(1):13-22.
476. Mowbray O, Krentzman AR, Bradley JC, Cranford JA, Robinson EAR, Grogan-Kaylor A. The effect of drinking goals at treatment entry on longitudinal alcohol use patterns among adults with alcohol dependence. *Drug Alcohol Depend.* 2013;132(1):182-188.
477. Berger L, Brondino M, Fisher M, Gwyther R, Garbutt JC. Alcohol use disorder treatment: the association of pretreatment use and the role of drinking goal. *J Am Board Fam Med.* 2016;29(1):37-49.
478. Dunn KE, EC S. Pretreatment alcohol drinking goals are associated with treatment outcomes. *Alcohol Clin Exp Res.* 2013;37(10):1745-1752.
479. Maisel NC, Blodgett JC, Wilbourne PL, Humphreys K, Finney JW. Meta-analysis of naltrexone and acamprosate for treating alcohol use disorders: when are these medications most helpful? *Addiction.* 2013;108(2):275-293. doi:10.1111/j.1360-0443.2012.04054.x
480. Henssler J, Muller M, Carreira J, Bschor T, Heinz A, Baethge C. Controlled drinking- non-abstinent versus abstinent treatment goals in alcohol use disorder: a systematic review, meta-analysis and meta-regression. *Addiction.* 2020;116(8):1973-1987.
481. Mann K, Aubin HJ, Witkiewitz K. Reduced Drinking in Alcohol Dependence Treatment, What Is the Evidence? *Eur Addict Res.* 2017;23(5):219-230. doi:10.1159/000481348
482. Yoo JE, Han K, Shin DW, et al. Association Between Changes in Alcohol Consumption and Cancer Risk. *JAMA network open.* 2022;5(8):e2228544-e2228544.
483. Witkiewitz K, Kranzler HR, Hallgren KA, et al. Stability of drinking reductions and long-term functioning among patients with alcohol use disorder. *J Gen Intern Med.* 2021;36(2):404-412.
484. Project Match Research Group. Matching Alcoholism Treatments to Client Heterogeneity: Project MATCH posttreatment drinking outcomes. *J Stud Alcohol.* 1997;58(1):7-29. doi:10.15288/jsa.1997.58.7
485. Stockwell T, Butt P, Beirness D, Gliksman L, Paradis C. The basis for Canada's new low-risk drinking guidelines: a relative risk approach to estimating hazardous levels and patterns of alcohol use. *Drug Alcohol Rev.* 2012;31(2):126-134. doi:10.1111/j.1465-3362.2011.00342.x

486. Rehm J, Roerecke M. Reduction of Drinking in Problem Drinkers and All-Cause Mortality. *Alcohol Alcohol*. 2013;48(4):509-513. doi:10.1093/alcalc/agt021
487. Roesner S, Hackl-Herrwerth A, Leucht S, Vecchi S, Srisurapanont M, Soyka M. Opioid antagonists for alcohol dependence. *Cochrane Database Syst Rev*. 2010;(12)Cd001867. doi:10.1002/14651858.CD001867.pub3
488. Center for Substance Abuse Treatment (CSAT), Substance Abuse and Mental Health Services Administration (SAMHSA). *Incorporating Alcohol Pharmacotherapies Into Medical Practice: A Treatment Improvement Protocol (TIP) 49*. HHS Publication No. (SMA) 09-4380. 2009. Accessed April 23, 2023. <https://store.samhsa.gov/product/TIP-49-Incorporating-Alcohol-Pharmacotherapies-Medical-Practice/SMA13-4380>
489. Cheng H, McGuinness LA, Elbers RG, et al. Treatment interventions to maintain abstinence from alcohol in primary care: Systematic review and network meta-analysis. *BMJ*. 2020;371:m3934.
490. Yen M-H, Ko H-C, Tang F-I, Lu R-B, Hong J-S. Study of hepatotoxicity of naltrexone in the treatment of alcoholism. *Alcohol*. 2006;38(2):117-120. doi:10.1016/j.alcohol.2006.05.003
491. Minozzi S, Amato L, Vecchi S, Davoli M, Kirchmayer U, Verster A. Oral naltrexone maintenance treatment for opioid dependence. *Cochrane Database Syst Rev*. 2011;(2):CD001333. doi:10.1002/14651858.CD001333.pub3
492. PrRevia™ (naltrexone hydrochloride) tablets, 50mg – Product Monograph. Teva Canada Limited. Available at: [https://pdf.hres.ca/dpd\\_pm/00030323.PDF](https://pdf.hres.ca/dpd_pm/00030323.PDF).
493. Roesner S, Hackl-Herrwerth A, Leucht S, Lehert P, Vecchi S, Soyka M. Acamprosate for alcohol dependence. *Cochrane Database Syst Rev*. 2010;(9)Cd004332. doi:10.1002/14651858.CD004332.pub2
494. Garbutt JC, Greenblatt AM, West SL, et al. Clinical and biological moderators of response to naltrexone in alcohol dependence: a Systematic review of the evidence. *Addiction*. 2014;109(8):1274-1284.
495. Monterosso JR, Flannery BA, Pettinati HM, et al. Predicting treatment response to naltrexone: the influence of craving and family history. *Am J Addict*. 2001;10(3):258-68.
496. Bogenschutz MP, Scott Tonigan J, Pettinati HM. Effects of Alcoholism Typology on Response to Naltrexone in the COMBINE Study. *Alcohol Clin Exp Res*. 2009;33(1):10-18. doi:10.1111/j.1530-0277.2008.00804.x
497. Anton RF, Latham PK, Voronin KE, et al. Nicotine-Use/Smoking Is Associated with the Efficacy of Naltrexone in the Treatment of Alcohol Dependence. Article. *Alcohol Clin Exp Res*. 2018;42(4):751-760. doi:10.1111/acer.13601
498. Schacht JP, Randall PK, Latham PK, et al. Predictors of Naltrexone Response in a Randomized Trial: Reward-Related Brain Activation, OPRM1 Genotype, and Smoking Status. *Neuropsychopharmacol*. 2017;42(13):2640-2653. doi:10.1038/npp.2017.74
499. Gueorguieva R, Wu R, Krystal JH, Donovan D, O'Malley SS. Temporal patterns of adherence to medications and behavioral treatment and their relationship to patient characteristics and treatment response. *Addict Behav*. 2013;38(5):2119-27. doi:10.1016/j.addbeh.2013.01.024

500. Zweben A, Pettinati HM, Weiss RD, et al. Relationship between medication adherence and treatment outcomes: the COMBINE study. *Alcohol Clin Exp Res*. 2008;32(9):1661-9. doi:10.1111/j.1530-0277.2008.00743.x
501. Kranzler HR, Armeli S, Tennen H, et al. Targeted naltrexone for early problem drinkers. *J Clin Psychopharmacol*. 2003;23(3):294-304. doi:10.1097/00004714-200306000-00010
502. Kranzler HR, Tennen H, Armeli S, et al. Targeted Naltrexone for Problem Drinkers. *J Clin Psychopharmacol*. 2009;29(4):350-357. doi:10.1097/JCP.0b013e3181ac5213
503. Kranzler HR, Tennen H, Penta C, Bohn MJ. Targeted naltrexone treatment of early problem drinkers. *Addict Behav*. 1997;22(3):431-436. doi:10.1016/s0306-4603(96)00064-0
504. Niciu MJ, Arias AJ. Targeted Opioid Receptor Antagonists in the Treatment of Alcohol Use Disorders. *CNS Drugs*. 2013;27(10):777-787. doi:10.1007/s40263-013-0096-4
505. Kalk NJ, Lingford Hughes AR. The clinical pharmacology of acamprosate. *Br J Clin Pharmacol*. 2014;77(2):315-323.
506. Mann K, Lehert P, Morgan MY. The efficacy of acamprosate in the maintenance of abstinence in alcohol-dependent individuals: results of a meta-analysis. *Alcohol Clin Exp Res*. 2004;28(1):51-63. doi:10.1097/01.alc.0000108656.81563.05
507. Mason BJ, Lehert P. Acamprosate for alcohol dependence: A sex-specific meta-analysis based on individual patient data. *Alcohol Clin Exp Res*. 2012;36(3):497-508.
508. Scott LJ, Figgitt DP, Keam SJ, Waugh J. Acamprosate - A review of its use in the maintenance of abstinence in patients with alcohol dependence. *CNS Drugs*. 2005;19(5):445-464. doi:10.2165/00023210-200519050-00006
509. Witkiewitz K, Saville K, Hamreus K. Acamprosate for treatment of alcohol dependence: Mechanisms, efficacy, and clinical utility. *Ther Clin Risk Manag*. 2012;8:45-53.
510. Kiefer F, Jahn H, Tarnaske T, et al. Comparing and combining naltrexone and acamprosate in relapse prevention of alcoholism: a double-blind, placebo-controlled study. *Arch Gen Psychiatry*. 2003;60(1):92-9.
511. Gual A, Lehert P. Acamprosate during and after acute alcohol withdrawal: a Double-blind placebo-controlled study in Spain. *Alcohol Alcohol*. 2001;36(5):413-418.
512. Tempesta E, Janiri L, Bignamini A, Chabac S, Potgieter A. Acamprosate and relapse prevention in the treatment of alcohol dependence: a Placebo-controlled study. *Alcohol Alcohol*. 2000;25(2):202-209.
513. Donoghue K, Elzerbi C, Saunders R, Whittington C, Pilling S, Drummond C. The efficacy of acamprosate and naltrexone in the treatment of alcohol dependence, Europe versus the rest of the world: a meta-analysis. *Addiction*. 2015;110(6):920-930. doi:10.1111/add.12875
514. Mason BJ, Goodman AM, Chabac S, Lehert P. Effect of oral acamprosate on abstinence in patients with alcohol dependence in a double-blind, placebo-controlled trial: the role of patient motivation. *J Psychiatr Res*. 2006;40(5):383-93. doi:10.1016/j.jpsychires.2006.02.002

515. Verheul R, Leher P, Geerlings PJ, Koeter MW, van den Brink W. Predictors of acamprosate efficacy: results from a pooled analysis of seven European trials including 1485 alcohol-dependent patients. *Psychopharmacology (Berl)*. 2005;178(2-3):167-73. doi:10.1007/s00213-004-1991-7
516. Rösner S, Leucht S, Leher P, Soyka M. Acamprosate supports abstinence, naltrexone prevents excessive drinking: evidence from a meta-analysis with unreported outcomes. *J Psychopharmacol*. 2008;22(1):11-23. doi:10.1177/0269881107078308
517. Hartung D, McCarty D, Fu R, Wiest K, Chalk M, Gastfriend DR. Extended-release Naltrexone for Alcohol and Opioid Dependence: A Meta-Analysis of Healthcare Utilization Studies. *J Subst Abuse Treat*. 2014;47(2):113-121. doi:10.1016/j.jsat.2014.03.007
518. Garbutt JC, Kranzler HR, O'Malley SS, et al. Efficacy and tolerability of long-acting injectable naltrexone for alcohol dependence: a randomized controlled trial. *JAMA*. 2005;293(13):1617-25. doi:10.1001/jama.293.13.1617
519. Murphy CE, Wang RC, Montoy JC, Whittaker E, Raven M. Effect of extended-release naltrexone on alcohol consumption: a Systematic review and meta-analysis. *Addiction*. 2021;
520. Jarvis BP, Holtyn AF, Subramaniam S, et al. Extended-release injectable naltrexone for opioid use disorder: a systematic review. *Addiction*. 2018;113(7):1188-1209. doi:10.1111/add.14180
521. Korthuis PT, Lum PJ, Vergara-Rodriguez P, et al. Feasibility and safety of extended-release naltrexone treatment of opioid and alcohol use disorder in HIV clinics: a pilot/feasibility randomized trial. *Addiction*. 2017;112(6):1036-44. doi:10.1111/add.13753
522. Nourredine M, Jurek L, Angerville B, et al. Use of topiramate in the spectrum of addictive and eating disorders: a Systematic review comparing treatment schemes, efficacy, and safety features *CNS Drugs*. 2021;35:177-213.
523. Blodgett JC, Del Re AC, Maisel NC, Finney JW. A meta-analysis of topiramate's effects for individuals with alcohol use disorders. *Alcohol Clin Exp Res*. 2014;38(6):1481-8. doi:10.1111/acer.12411
524. Johnson BA, Ait-Daoud N, Bowden CL, et al. Oral topiramate for treatment of alcohol dependence: a randomised controlled trial. *Lancet*. 2003;361(9370):1677-85. doi:10.1016/S0140-6736(03)13370-3
525. Johnson BA, Rosenthal N, Capece JA, et al. Topiramate for treating alcohol dependence: a randomized controlled trial. *JAMA*. 2007;298(14):1641-51. doi:10.1001/jama.298.14.1641
526. Kranzler HR, Covault J, Feinn R, et al. Topiramate treatment for heavy drinkers: moderation by a GRIK1 polymorphism. *Am J Psychiat*. 2014;171(4):445-52. doi:10.1176/appi.ajp.2013.13081014
527. Kampman KM, Pettinati HM, Lynch KG, Spratt K, Wierzbicki MR, O'Brien CP. A double-blind, placebo-controlled trial of topiramate for the treatment of comorbid cocaine and alcohol dependence. *Drug Alcohol Depend*. 2013;133(1):94-99. doi:10.1016/j.drugalcdep.2013.05.026

528. Likhitsathian S, Uttawichai K, Booncharoen H, Wittayanookulluk A, Angkurawaranon C, Srisurapanont M. Topiramate treatment for alcoholic outpatients recently receiving residential treatment programs: A 12-week, randomized, placebo-controlled trial. *Drug Alcohol Depend*. 2013;133(2):440-446. doi:10.1016/j.drugalcdep.2013.06.032
529. Baltieri DA, Daró FR, Ribeiro PL, de Andrade AG. Comparing topiramate with naltrexone in the treatment of alcohol dependence. *Addiction*. 2008;103(12):2035-44. doi:10.1111/j.1360-0443.2008.02355.x
530. Rubio G, Martínez-Gras I, Manzanares J. Modulation of impulsivity by topiramate: implications for the treatment of alcohol dependence. *J Clin Psychopharm*. 2009;29(6):584-9. doi:10.1097/JCP.0b013e3181bfdb79
531. Flórez G, García-Portilla P, Alvarez S, Saiz PA, Nogueiras L, Bobes J. Using topiramate or naltrexone for the treatment of alcohol-dependent patients. *Alcohol Clin Exp Res*. 2008;32(7):1251-9. doi:10.1111/j.1530-0277.2008.00680.x
532. Flórez G, Saiz PA, García-Portilla P, Alvarez S, Nogueiras L, Bobes J. Topiramate for the treatment of alcohol dependence: comparison with naltrexone. *Eur Addict Res*. 2011;17(1):29-36. doi:10.1159/000320471
533. Paparrigopoulos T, Tzavellas E, Karaiskos D, Kourlaba G, Liappas I. Treatment of alcohol dependence with low-dose topiramate: an open-label controlled study. *BMC Psychiatry*. 2011;11:41. doi:10.1186/1471-244X-11-41
534. Kranzler HR, Feinn R, Morris P, Hartwell EE. A meta-analysis of the efficacy of gabapentin for treating alcohol use disorder. *Addiction*. 2019;114(9):1547-1555. doi:10.1111/add.14655
535. Ahmed S, Bachu R, Kotapati P, et al. Use of Gabapentin in the Treatment of Substance Use and Psychiatric Disorders: A Systematic Review. *Frontiers in psychiatry Frontiers Research Foundation*. 2019;10:228. doi:<https://dx.doi.org/10.3389/fpsy.2019.00228>
536. Anton RF, Latham P, Voronin K, et al. Efficacy of Gabapentin for the Treatment of Alcohol Use Disorder in Patients With Alcohol Withdrawal Symptoms: A Randomized Clinical Trial. *JAMA Internal Medicine*. 2020;180(5):728-736. doi:<https://dx.doi.org/10.1001/jamainternmed.2020.0249>
537. Mason BJ, Quello S, Shadan F. Gabapentin for the treatment of alcohol use disorder. *Expert Opin Inv Drugs*. 2018;27(1):113-124. doi:10.1080/13543784.2018.1417383
538. Falk DE, Ryan ML, Fertig JB, et al. Gabapentin Enacarbil Extended-Release for Alcohol Use Disorder: A Randomized, Double-Blind, Placebo-Controlled, Multisite Trial Assessing Efficacy and Safety. *Alcohol Clin Exp Res*. 2019;43(1):158-169. doi:10.1111/acer.13917
539. Wiffen PJ, Derry S, Bell RF, et al. Gabapentin for chronic neuropathic pain in adults. *Cochrane Database Syst Rev*. 2017;(6)Cd007938. doi:10.1002/14651858.CD007938.pub4
540. Raouf M, Atkinson TJ, Crumb MW, Fudin J. Rational dosing of gabapentin and pregabalin in chronic kidney disease. *J Pain Res*. 2017;10:275-278. doi:10.2147/jpr.s130942
541. Howland RH. Gabapentin for Substance Use Disorders: Is it Safe and Appropriate? *J Psychosoc Nurs Men*. 2014;1-4. doi:10.3928/02793695-20131217-01

542. Howland RH. Gabapentin: can it be misused? *J Psychosoc Nurs Men*. 2014;52(1):12-5.
543. Schifano F. Misuse and abuse of pregabalin and gabapentin: cause for concern? *CNS Drugs*. 2014;28(6):491-6. doi:10.1007/s40263-014-0164-4
544. Smith RV, Havens JR, Walsh SL. Gabapentin misuse, abuse and diversion: a systematic review. *Addiction*. 2016;111(7):1160-74. doi:10.1111/add.13324
545. Peckham AM, Fairman KA, Sclar DA. Policies to mitigate nonmedical use of prescription medications: how should emerging evidence of gabapentin misuse be addressed? *Expert Opin Drug Saf*. 2018;17(5):519-523. doi:10.1080/14740338.2017.1390081
546. Evoy KE, Morrison MD, Saklad SR. Abuse and Misuse of Pregabalin and Gabapentin. *Drugs*. 2017;77(4):403-426. doi:10.1007/s40265-017-0700-x
547. Kapil V, Green JL, Le Lait MC, Wood DM, Dargan PI. Misuse of the  $\gamma$ -aminobutyric acid analogues baclofen, gabapentin and pregabalin in the UK. *Br J Clin Pharmacol*. 2014;78(1):190-1.
548. Peckham AM, Evoy KE, Covvey JR, Ochs L, Fairman KA, Sclar DA. Predictors of Gabapentin Overuse With or Without Concomitant Opioids in a Commercially Insured US Population. *Pharmacotherapy*. 2018;38(4):436-443. doi:10.1002/phar.2096
549. Wilens T, Zulauf C, Ryland D, Carrellas N, Catalina-Wellington I. Prescription medication misuse among opioid dependent patients seeking inpatient detoxification. *Am J Addict*. 2015;24(2):173-7. doi:10.1111/ajad.12159
550. Grosshans M, Lemenager T, Vollmert C, et al. Pregabalin abuse among opiate addicted patients. *Eur J Clin Pharmacol*. 2013;69(12):2021-5. doi:10.1007/s00228-013-1578-5
551. Reccoppa L, Malcolm R, Ware M. Gabapentin abuse in inmates with prior history of cocaine dependence. *Am J Addict*. 2004;13(3):321-323. doi:10.1080/10550490490460300
552. Mersfelder TL, Nichols WH. Gabapentin: Abuse, Dependence, and Withdrawal. *Ann Pharmacother*. 2016;50(3):229-33. doi:10.1177/1060028015620800
553. Bastiaens L, Galus J, Mazur C. Abuse of Gabapentin is Associated with Opioid Addiction. *Psychiatr Q*. 2016;87(4):763-767. doi:10.1007/s11126-016-9421-7
554. Reeves RR, Ladner ME. Potentiation of the effect of buprenorphine/naloxone with gabapentin or quetiapine. *Am J Psychiatr*. 2014;171(6):691. doi:10.1176/appi.ajp.2014.13111526
555. Baird CR, Fox P, Colvin LA. Gabapentinoid abuse in order to potentiate the effect of methadone: a survey among substance misusers. *Eur Addict Res*. 2014;20(3):115-8. doi:10.1159/000355268
556. Reeves RR, Burke RS. Abuse of combinations of gabapentin and quetiapine. *Prim Care Companion CNS Disord*. 2014;16(5)doi:10.4088/PCC.14l01660

557. Health Canada. Health Canada Advises Canadians to Exercise Caution when Taking Gabapentin or Pregabalin with Opioids. <https://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2019/71003a-eng.php>
558. Lyndon A, Audrey S, Wells C, et al. Risk to heroin users of polydrug use of pregabalin or gabapentin. *Addiction*. 2017;112(9):1580-1589. doi:10.1111/add.13843
559. Gomes T, Juurlink DN, Antoniou T, Mamdani MM, Paterson JM, van den Brink W. Gabapentin, opioids, and the risk of opioid-related death: A population-based nested case-control study. *PLoS Med*. 2017;14(10)e1002396. doi:10.1371/journal.pmed.1002396
560. Slavova S, Miller A, Bunn TL, et al. Prevalence of gabapentin in drug overdose postmortem toxicology testing results. *Drug Alcohol Depend*. 2018;186:80-85. doi:10.1016/j.drugalcdep.2018.01.018
561. Odyssey Pharmaceuticals, Inc. Antabuse (disulfiram) tablets prescribing information. East Hanover, NJ; 2003. Available at: <https://www.drugs.com/monograph/disulfiram.html>.
562. Fuller RK, Branchey L, Brightwell DR, et al. Disulfiram treatment of alcoholism. *JAMA*. 1986;256(11):1449-1455. doi:10.1001/jama.256.11.1449
563. Skinner MD, Lahmek P, Pham H, Aubin HJ. Disulfiram efficacy in the treatment of alcohol dependence: a meta-analysis. *PLoS ONE*. 2014;9(2):e87366. doi:10.1371/journal.pone.0087366
564. Laaksonen E, Koski-Jannes A, Salaspuro M, Ahtinen H, Alho H. A randomized, multicentre, open-label, comparative trial of disulfiram, naltrexone and acamprosate in the treatment of alcohol dependence. *Alcohol Alcohol*. 2008;43(1):53-61. doi:10.1093/alcalc/agg136
565. O'Farrell TJ, Schein AZ. Behavioral Couples Therapy for Alcoholism and Drug Abuse. *Journal of Family Psychotherapy*. 2011;22(3):193-215. doi:10.1080/08975353.2011.602615
566. Rolland B, Simon N, Franchitto N. Safety Challenges of Using High Dose Baclofen for Alcohol Use Disorder: A Focused Review. *Front Psychiatr*. 2018;9:367. doi:10.3389/fpsyt.2018.00367
567. Rolland B, Paille F, Gillet C, et al. Pharmacotherapy for Alcohol Dependence: The 2015 Recommendations of the French Alcohol Society, Issued in Partnership with the European Federation of Addiction Societies. *CNS Neurosci Ther*. 2016;22(1):25-37. doi:10.1111/cns.12489
568. Addolorato G, Caputo F, Capristo E, et al. Baclofen efficacy in reducing alcohol craving and intake: a preliminary double-blind randomized controlled study. *Alcohol Alcohol*. 2002;37(5):504-8.
569. Addolorato G, Leggio L, Ferrulli A, et al. Effectiveness and safety of baclofen for maintenance of alcohol abstinence in alcohol-dependent patients with liver cirrhosis: randomised, double-blind controlled study. *Lancet*. 2007;370(9603):1915-22. doi:10.1016/S0140-6736(07)61814-5
570. Beraha EM, Salemink E, Goudriaan AE, et al. Efficacy and safety of high-dose baclofen for the treatment of alcohol dependence: A multicentre, randomised, double-blind controlled trial. *Eur Neuropsychopharm*. 2016;26(12):1950-1959. doi:10.1016/j.euroneuro.2016.10.006



571. Garbutt JC, Kampov-Polevoy AB, Gallop R, Kalka-Juhl L, Flannery BA. Efficacy and Safety of Baclofen for Alcohol Dependence: A Randomized, Double-Blind, Placebo-Controlled Trial. *Alcohol Clin Exp Res*. 2010;34(11):1849-1857. doi:10.1111/j.1530-0277.2010.01273.x
572. Hauser P, Fuller B, Ho SB, Thuras P, Kern S, Dieperink E. The safety and efficacy of baclofen to reduce alcohol use in veterans with chronic hepatitis C: a randomized controlled trial. *Addiction*. 2017;112(7):1173-1183. doi:10.1111/add.13787
573. Ponizovsky AM, Rosca P, Aronovich E, Weizman A, Grinshpoon A. Baclofen as Add-On to Standard Psychosocial Treatment for Alcohol Dependence: a Randomized, Double-Blind, Placebo-Controlled Trial With 1 Year Follow-Up. *J Subst Abuse Treat*. 2015;52:24-30. doi:10.1016/j.jsat.2014.11.007
574. Rigal L, Sidorkiewicz S, Tréluyer JM, et al. Titrated baclofen for high-risk alcohol consumption: a randomized placebo-controlled trial in out-patients with 1-year follow-up. *Addiction*. 2020;115(7):1265-1276. doi:10.1111/add.14927
575. Agabio R, Saulle R, Rösner S, Minozzi S. Baclofen for alcohol use disorder. *Cochrane Database Syst Rev*. 2023;1(1):Cd012557. doi:10.1002/14651858.CD012557.pub3
576. Pierce M, Sutherland A, Beraha EM, Morley K, van den Brink W. Efficacy, tolerability, and safety of low-dose and high-dose baclofen in the treatment of alcohol dependence: A systematic review and meta-analysis. *Eur Neuropsychopharm*. 2018;28(7):795-806. doi:10.1016/j.euroneuro.2018.03.017
577. Rose AK, Jones A. Baclofen: its effectiveness in reducing harmful drinking, craving, and negative mood. A meta-analysis. *Addiction*. 2018;113(8):1396-1406. doi:10.1111/add.14191
578. Agabio R, Baldwin DS, Amaro H, Leggio L, JMA S. The influence of anxiety symptoms on clinical outcome during baclofen treatment of alcohol use disorder: a Systematic review and meta-analysis. *Neurosci Biobehav Rev*. 2021;125:296-313.
579. Bschor T, Henssler J, Muller M, Baethge C. Baclofen for alcohol use disorder: a systematic meta-analysis. *Acta Psychiatr Scand*. 2018;138(3):232-242. doi:10.1111/acps.12905
580. Minozzi S, Saulle R, Rosner S. Baclofen for alcohol use disorder. *Cochrane Database Syst Rev*. 2018;11:CD012557. doi:10.1002/14651858.CD012557.pub2
581. Auffret M, Labreuche J, Duhamel A, et al. Proactive Regional Pharmacovigilance System Versus National Spontaneous Reporting for Collecting Safety Data on Concerning Off-Label Prescribing Practices: An Example with Baclofen and Alcohol Dependence in France. *Drug Saf*. 2017;40(3):257-262. doi:10.1007/s40264-016-0489-7
582. Chaignot C, Zureik M, Rey G, Dray-Spira R, Coste J, Weill A. Risk of hospitalisation and death related to baclofen for alcohol use disorders: Comparison with nalmefene, acamprosate, and naltrexone in a cohort study of 165 334 patients between 2009 and 2015 in France. *Pharmacoepidemiol Drug Safety*. 2018;27(11):1239-1248. doi:10.1002/pds.4635

583. Ye JH, Ponnudurai R, Schaefer R. Ondansetron: A selective 5-HT<sub>3</sub> receptor antagonist and its applications in CNS-Related disorders. *CNS Drug Reviews*. 2001;7(2):199-213.
584. Johnson BA, Roache JD, Javors MA, et al. Ondansetron for reduction of drinking among biologically predisposed alcoholic patients - A randomized controlled trial. *JAMA*. 2000;284(8):963-971. doi:10.1001/jama.284.8.963
585. Johnson BA, Ait-Daoud N, Seneviratne C, et al. Pharmacogenetic Approach at the Serotonin Transporter Gene as a Method of Reducing the Severity of Alcohol Drinking. *Am J Psychiat*. 2011;168(3):265-275. doi:10.1176/appi.ajp.2010.10050755
586. Yardley MM, Ray LA. Medications development for the treatment of alcohol use disorder: insights into the predictive value of animal and human laboratory models. *Addict Biol*. 2017;22(3):581-615. doi:10.1111/adb.12349
587. Sellers EM, Toneatto T, Romach MK, Somer GR, Sobell LC, Sobell MB. Clinical efficacy of the 5-HT<sub>3</sub> antagonist ondansetron in alcohol-abuse and dependence. *Alcohol Clin Exp Res*. 1994;18(4):879-885. doi:10.1111/j.1530-0277.1994.tb00054.x
588. Freedman SB, Uleryk E, Rumantir M, Finkelstein Y. Ondansetron and the Risk of Cardiac Arrhythmias: A Systematic Review and Postmarketing Analysis. *Ann Emerg Med*. 2014;64(1):19-25. doi:10.1016/j.annemergmed.2013.10.026
589. Doggrell SA, Hancox JC. Cardiac safety concerns for ondansetron, an antiemetic commonly used for nausea linked to cancer treatment and following anaesthesia. *Expert Opin Drug Saf*. 2013;12(3):421-431. doi:10.1517/14740338.2013.780026
590. Naglich AC, Lin A, Wakhlu S, Adinoff BH. Systematic Review of Combined Pharmacotherapy for the Treatment of Alcohol Use Disorder in Patients Without Comorbid Conditions. *CNS Drugs*. 2018;32(1):13-31. doi:10.1007/s40263-017-0484-2
591. Anton RF, Myrick H, Wright TM, et al. Gabapentin Combined With Naltrexone for the Treatment of Alcohol Dependence. *Am J Psychiat*. 2011;168(7):709-717. doi:10.1176/appi.ajp.2011.10101436
592. Jones JD, Comer SD, Kranzler HR. The Pharmacogenetics of Alcohol Use Disorder. *Alcohol Clin Exp Res*. 2015;39(3):391-402. doi:10.1111/acer.12643
593. Kim SG, Kim CM, Choi SW, et al. A mu opioid receptor gene polymorphism (A118G) and naltrexone treatment response in adherent Korean alcohol-dependent patients. *Psychopharmacology (Berl)*. 2009;201(4):611-618. doi:10.1007/s00213-008-1330-5
594. Oslin DW, Berrettini W, Kranzler HR, et al. A functional polymorphism of the mu-opioid receptor gene is associated with naltrexone response in alcohol-dependent patients. *Neuropsychopharmacol*. 2003;28(8):1546-1552. doi:10.1038/sj.npp.1300219
595. Anton RF, Oroszi G, O'Malley S, et al. An evaluation of mu-opioid receptor (OPRM1) as a predictor of naltrexone response in the treatment of alcohol dependence. *Arch Gen Psychiatry*. 2008;65(2):135-144. doi:10.1001/archpsyc.65.2.135

596. Ray LA, Bujarski S, Chin PF, Miotto K. Pharmacogenetics of naltrexone in asian americans: a Randomized placebo-controlled laboratory study. *Neuropsychopharmacology*. 2012;37(2):445-455.
597. Oslin DW, Leong SH, Lynch KG, et al. Naltrexone vs Placebo for the Treatment of Alcohol Dependence: A Randomized Clinical Trial. *JAMA Psychiatry*. 2015;72(5):430-7. doi:10.1001/jamapsychiatry.2014.3053
598. Pharmacogenomics and Pharmacometabolomics of Acamprosate Treatment Outcome. Posted January 28, 2019. Updated August 14, 2019. Accessed April 3, 2020. <https://ClinicalTrials.gov/show/NCT03818191>
599. Adverse Childhood Experiences in Substance-related Disorders. Updated January 17, 2019. Accessed April 3, 2020. <https://ClinicalTrials.gov/show/NCT03758053>
600. Leveraging Biomarkers for Personalized Treatment of Alcohol Use Disorder Comorbid With PTSD. Updated November 19, 2019. Accessed April 3, 2020. <https://ClinicalTrials.gov/show/NCT03667846>
601. Pharmacogenetic Study of Ondansetron in Alcohol Use Disorder. Updated September 26, 2019. Accessed April 3, 2020. <https://ClinicalTrials.gov/show/NCT02354703>
602. The Effect of NK1R Antagonism on Alcohol Craving and PTSD Symptoms in Alcohol Dependent Patients With PTSD. Updated November 3, 2015. Accessed April 3, 2020. <https://ClinicalTrials.gov/show/NCT00896038>
603. Leung JG, Hall-Flavin D, Nelson S, Schmidt KA, Schak KM. The role of gabapentin in the management of alcohol withdrawal and dependence. Review. *Ann Pharmacother*. 2015;49(8):897-906. doi:10.1177/1060028015585849
604. Reus VI, Fochtmann LJ, Bukstein O, et al. The American Psychiatric Association Practice Guideline for the Pharmacological Treatment of Patients With Alcohol Use Disorder. *Am J Psychiat*. 2018;175(1):86-90. doi:10.1176/appi.ajp.2017.1750101
605. Kranzler HR, Soyka M. Diagnosis and Pharmacotherapy of Alcohol Use Disorder: A Review. *JAMA*. 2018;320(8):815-824. doi:10.1001/jama.2018.11406
606. Dawes MA, Johnson BA. Pharmacotherapeutic trials in adolescent alcohol use disorders: opportunities and challenges. *Alcohol Alcohol*. 2004;39(3):166-177. doi:10.1093/alcalc/agh045
607. Brown SA, McGue M, Maggs J, et al. A developmental perspective on alcohol and youths 16 to 20 years of age. *Pediatrics*. 2008;121(Suppl 4):S290-S310. doi:10.1542/peds.2007-2243D
608. Deas D, May K, Randall C, Johnson N, Anton R. Naltrexone treatment of adolescent alcoholics: An open-label pilot study. *J Child Adolesc Psychopharmacol*. 2005;15(5):723-728. doi:10.1089/cap.2005.15.723
609. Miranda R, Ray L, Blanchard A, et al. Effects of naltrexone on adolescent alcohol cue reactivity and sensitivity: an initial randomized trial. *Addict Biol*. 2014;19(5):941-954. doi:10.1111/adb.12050
610. De Sousa AA, De Sousa J, Kapoor H. An open randomized trial comparing disulfiram and topiramate in the treatment of alcohol dependence. *J Subst Abuse Treat*. 2008;34(4):460-3. doi:10.1016/j.jsat.2007.05.012

611. De Sousa A. A comparative study using Disulfiram and Naltrexone in alcohol-dependent adolescents. *J Subst Use*. 2014;19(5):341-345. doi:10.3109/14659891.2013.813084
612. Lingford-Hughes AR, Welch S, Peters L, et al. BAP updated guidelines: evidence-based guidelines for the pharmacological management of substance abuse, harmful use, addiction and comorbidity: recommendations from BAP. *J Psychopharmacol*. 2012;26(7):899-952. doi:10.1177/0269881112444324
613. Royal College of General Practitioners, Alcohol Concern, DrugScope, Royal College of Psychiatrists, College Centre for Quality Improvement (CCQI). *Practice Standards for Young People with Substance Misuse Problems*. Publication number CCQI 127. Published June 2012. Accessed April 7, 2020. [http://www.emcdda.europa.eu/attachements.cfm/att\\_232130\\_EN\\_UK58\\_Practice%20standards%20for%20young%20people%20with%20substance%20misuse%20problems%20\(2012\).pdf](http://www.emcdda.europa.eu/attachements.cfm/att_232130_EN_UK58_Practice%20standards%20for%20young%20people%20with%20substance%20misuse%20problems%20(2012).pdf)
614. McDonald PLL, Jia LS, Vipler S. Alcohol Withdrawal Management and Relapse Prevention in Pregnancy. *Can J Addiction*. 2018;9(4):32-41. doi:10.1097/cxa.0000000000000034
615. Jones CW, Terplan M. Pregnancy and Naltrexone Pharmacotherapy. *Obstetrics & Gynecology*. 2018;132(4):923-925. doi:10.1097/aog.0000000000002864
616. Vickers AP, Jolly A. Naltrexone and problems in pain management. *Bmj*. 2006;332(7534):132-3. doi:10.1136/bmj.332.7534.132
617. Chan CF, Page-Sharp M, Kristensen JH, O'Neil G, Ilett KF. Transfer of Naltrexone and its Metabolite 6, B-Naltrexol into Human Milk. *J Hum Lact*. 2004;20(3):322-326.
618. Hunt S, Russell A, Smithson WH, et al. Topiramate in pregnancy: preliminary experience from the UK Epilepsy and Pregnancy Register. *Neurology*. 2008;71(4):272-6. doi:10.1212/01.wnl.0000318293.28278.33
619. Oslin D, Liberto JG, O'Brien J, Krois S, Norbeck J. Naltrexone as an adjunctive treatment for older patients with alcohol dependence. *Am J Geriatr Psychiatry*. 1997;5(4):324-332.
620. Abuse SAaMHSAAaNIoA, Alcoholism a. *Medication for the Treatment of Alcohol Use Disorder: A Brief Guide*. 2015. 2015. Accessed March 7, 2023. <https://store.samhsa.gov/sites/default/files/d7/priv/sma15-4907.pdf>
621. Anton RF, Moak DH, Latham P, et al. Naltrexone combined with either cognitive behavioral or motivational enhancement therapy for alcohol dependence. *J Clin Psychopharm*. 2005;25(4):349-57.
622. Gao J, Cao J, Guo T, Xiao Y. Association between alcoholic interventions and abstinence rates for alcohol use disorders: A meta-analysis. *Medicine (Baltimore)*. 2018;97(50):e13566. doi:<https://dx.doi.org/10.1097/MD.00000000000013566>
623. Ray LA, Meredith LR, Kiluk BD, Walthers J, Carroll KM, Magill M. Combined Pharmacotherapy and Cognitive Behavioral Therapy for Adults With Alcohol or Substance Use Disorders: A Systematic Review and Meta-analysis. *JAMA Netw Open*. 2020;3(6):e208279. doi:10.1001/jamanetworkopen.2020.8279
624. PrCampral® (acamprosate calcium) delayed release tablets, 333mg – Product Monograph. Mylan Pharmaceuticals ULC. Available at: [https://pdf.hres.ca/dpd\\_pm/00014184.PDF](https://pdf.hres.ca/dpd_pm/00014184.PDF).

625. PrTopamax® (topiramate) tablets, House Std., 25, 100, 200mg; topiramate sprinkle capsules, House Std. 15, 25mg – Product Monograph. Janssen Inc. Available at: [https://pdf.hres.ca/dpd\\_pm/00046099.PDF](https://pdf.hres.ca/dpd_pm/00046099.PDF).
626. PrNEURONTIN® Product Monograph – Gabapentin Capsules 100 mg, 300 mg, and 400 mg; Tablets 600 mg and 800 mg. Submission Control No: 211678. Pfizer Canada Ltd. Available at: [https://pdf.hres.ca/dpd\\_pm/00044022.PDF](https://pdf.hres.ca/dpd_pm/00044022.PDF).
627. Glass JE, Williams EC, Bucholz KK. Psychiatric Comorbidity and Perceived Alcohol Stigma in a Nationally Representative Sample of Individuals with DSM-5 Alcohol Use Disorder. *Alcohol Clin Exp Res*. 2014;38(6):1697-1705. doi:10.1111/acer.12422
628. Hassan AN. Patients With Alcohol Use Disorder Co-Occurring With Depression and Anxiety Symptoms: Diagnostic and Treatment Initiation Recommendations. *J Clin Psychiat*. 2018;79(1)doi:10.4088/JCP.17ac11999
629. Kingston REF, Marel C, Mills KL. A systematic review of the prevalence of comorbid mental health disorders in people presenting for substance use treatment in Australia. *Drug Alcohol Rev*. 2017;36(4):527-539. doi:10.1111/dar.12448
630. Substance Abuse and Mental Health Services Administration (SAMHSA). *Key substance use and mental health indicators in the United States: Results from the 2017 National Survey on Drug Use and Health*. HHS Publication No. SMA 18-5068, NSDUH Series H-53. Center for Behavioral Health Statistics and Quality, SAMHSA; 2017. Accessed April 8, 2020. <https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHFFR2017/NSDUHFFR2017.pdf>
631. Karapareddy V. A review of integrated care for concurrent disorders: cost effectiveness and clinical outcomes. *J Dual Diagn*. 2018;15(1):56-66.
632. Driessen M, Meier S, Hill A, Wetterling T, Lange W, Junghanns K. The course of anxiety, depression and drinking behaviours after completed detoxification in alcoholics with and without comorbid anxiety and depressive disorders. *Alcohol Alcohol*. 2001;36(3):249-255. doi:10.1093/alcalc/36.3.249
633. McHugh RK, Sugarman DE, Meyer L, Fitzmaurice GM, Greenfield SF. The relationship between perceived stress and depression in substance use disorder treatment. *Drug Alcohol Depend*. 2020;207:107819. doi:<https://doi.org/10.1016/j.drugalcdep.2019.107819>
634. Brown SA, Irwin M, Schuckit MA. Changes in anxiety among abstinent male alcoholics. *J Stud Alcohol*. 1991;52(1):55-61.
635. Brown SA, Schuckit MA. Changes in depression among abstinent alcoholics. *J Stud Alcohol*. 1988;49(5):412-417.
636. Liappas J, Paparrigopoulos T, Tzavellas E, Christodoulou G. Impact of alcohol detoxification on anxiety and depressive symptoms. *Drug Alcohol Depend*. 2002;68(2):215-220. doi:[https://doi.org/10.1016/S0376-8716\(02\)00195-3](https://doi.org/10.1016/S0376-8716(02)00195-3)
637. Torrens M, Fonseca F, Mateu G, Farre M. Efficacy of antidepressants in substance use disorders with and without comorbid depression. A systematic review and meta-analysis. *Drug Alcohol Depend*. 2005;78(1):1-22.

638. Eriksson M, Berggren U, Blennow K, Fahlke C, Balldin J. Further investigation of citalopram on alcohol consumption in heavy drinkers: responsiveness possibly linked to the DRD2 A2/A2 genotype. *Alcohol*. 2001;24(1):15-23.
639. Kenna GA, Zywiak WH, McGeary JE, et al. A within-group design of nontreatment seeking 5-HTTLPR genotyped alcohol-dependent subjects receiving ondansetron and sertraline. *Alcoholism: Clinical & Experimental Research*. 2009;33(2):315-323. doi:<https://dx.doi.org/10.1111/j.1530-0277.2008.00835.x>
640. Charney DA, Heath LM, Zikos E, Palacios-Boix J, Gill KJ. Poorer Drinking Outcomes with Citalopram Treatment for Alcohol Dependence: A Randomized, Double-Blind, Placebo-Controlled Trial. *Alcohol Clin Exp Res*. 2015;39(9):1756-65. doi:10.1111/acer.12802
641. Ballesta A, Orio L, Arco R, et al. Bupropion, a possible antidepressant without negative effects on alcohol relapse. *Eur Neuropsychopharmacol*. 2019;29(6):756-765. doi:<https://doi.org/10.1016/j.euroneuro.2019.03.012>
642. Alén F, Orio L, Gorriti MÁ, et al. Increased alcohol consumption in rats after subchronic antidepressant treatment. *Int J Neuropsychopharmacol*. 2013;16(8):1809-1818. doi:10.1017/s1461145713000217
643. Kranzler HR, Armeli S, Tennen H, et al. A double-blind, randomized trial of sertraline for alcohol dependence: Moderation by age of onset [corrected] and 5-hydroxytryptamine transporter-linked promoter region genotype. *Psychopharmacol*. 2011;31(1):22-30.
644. Kranzler HR, Armeli S, Tennen H. Post-treatment outcomes in a double-blind, randomized trial of sertraline for alcohol dependence. *Alcoholism: Clinical & Experimental Research*. 2012;36(4):739-744. doi:<https://dx.doi.org/10.1111/j.1530-0277.2011.01659.x>
645. Geoffroy PA, Lejoyeux M, Rolland B. Management of insomnia in alcohol use disorder. Review. *Expert Opin Pharmacother*. 2020;21(3):297-306. doi:<http://dx.doi.org/10.1080/14656566.2019.1705279>
646. Agabio R, Trogu E, Pani PP. Antidepressants for the treatment of people with co-occurring depression and alcohol dependence. *Cochrane Database Syst Rev*. 2018;(4)
647. Iovieno N, Tedeschini E, Bentley KH, Evins AE, Papakostas GI. Antidepressants for major depressive disorder and dysthymic disorder in patients with comorbid alcohol use disorders: a Meta-analysis of placebo-controlled randomized trials. *J Clin Psychiatry*. 2011;72(8):1144-1151.
648. Grant S, Azhar G, Han E, et al. Clinical interventions for adults with comorbid alcohol use and depressive disorders: A systematic review and network meta-analysis. *PLoS Medicine / Public Library of Science*. 2021;18(10):e1003822. doi:<https://dx.doi.org/10.1371/journal.pmed.1003822>
649. Torrens M, Tirado-Muñoz J, Fonseca F, et al. Clinical practice guideline on pharmacological and psychological management of adult patients with depression and a comorbid substance use disorder. *Adicciones*. 2022;34(2):128-141. Guía de práctica clínica para el tratamiento farmacológico y psicológico de los pacientes adultos con depresión y un diagnóstico comórbido de trastorno por uso de sustancias. doi:10.20882/adicciones.1559
650. Deas D, Randall CL, Roberts JS, Anton RF. A double-blind, placebo-controlled trial of sertraline in depressed adolescent alcoholics: a pilot study. *Hum Psychopharmacol*. 2000;15(6):461-469.

651. Cornelius JR, Bukstein OG, Wood DS, Kirisci L, Douaihy A, Clark DB. Double-blind placebo-controlled trial of fluoxetine in adolescents with comorbid major depression and an alcohol use disorder. *Addict Behav.* 2009;34(10):905-909. doi:<https://dx.doi.org/10.1016/j.addbeh.2009.03.008>
652. Adamson SJ, Sellman JD, Foulds JA, et al. A Randomized Trial of Combined Citalopram and Naltrexone for Nonabstinent Outpatients With Co-Occurring Alcohol Dependence and Major Depression. *J Clin Psychopharmacol.* 2015;35(2):143-149. doi:10.1097/jcp.0000000000000287
653. Pettinati HM, Oslin DW, Kampman KM, et al. A double-blind, placebo-controlled trial combining sertraline and naltrexone for treating co-occurring depression and alcohol dependence. *Am J Psychiatry.* 2010;167(6):668-75. doi:10.1176/appi.ajp.2009.08060852
654. Krystal JH, Gueorguieva R, Cramer J, Collins J, Rosenheck R, Team TVCNS. Naltrexone Is Associated With Reduced Drinking by Alcohol Dependent Patients Receiving Antidepressants for Mood and Anxiety Symptoms: Results From VA Cooperative Study No. 425, "Naltrexone in the Treatment of Alcoholism". *Alcoholism: Clinical and Experimental Research.* 2008;32(1):85-91. doi:<https://doi.org/10.1111/j.1530-0277.2007.00555.x>
655. Levinson W, Huynh T. Engaging physicians and patients in conversations about unnecessary tests and procedures: Choosing Wisely Canada. *CMAJ.* 2014;186(5):325-6. doi:10.1503/cmaj.131674
656. Ipser JC, Wilson D, Akindipe TO, Sager C, Stein DJ. Pharmacotherapy for anxiety and comorbid alcohol use disorders. *Cochrane Database Syst Rev.* 2015;(1)doi:10.1002/14651858.CD007505.pub2
657. Ciraulo DA, Barlow DH, Gulliver SB, et al. The effects of venlafaxine and cognitive behavioral therapy alone and combined in the treatment of co-morbid alcohol use-anxiety disorders. *Behav Res Ther.* 2013;51(11):729-735.
658. Moss HB, Goldstein RB, Chen CM, Yi HY. Patterns of use of other drugs among those with alcohol dependence: Associations with drinking behavior and psychopathology. *Addict Behav.* 2015;50:192-8. doi:10.1016/j.addbeh.2015.06.041
659. Saha TD, Grant BF, Chou SP, Kerridge BT, Pickering RP, Ruan WJ. Concurrent use of alcohol with other drugs and DSM-5 alcohol use disorder comorbid with other drug use disorders: Sociodemographic characteristics, severity, and psychopathology. *Drug Alcohol Depend.* 2018;187:261-269. doi:10.1016/j.drugalcdep.2018.03.006
660. McCabe SE, West BT, Jutkiewicz EM, Boyd CJ. Multiple DSM-5 substance use disorders: A national study of US adults. *Hum Psychopharmacol.* 2017;32(5):e2625. doi:10.1002/hup.2625
661. Levin FR, Mariani J, Brooks DJ, et al. A randomized double-blind, placebo-controlled trial of venlafaxine-extended release for co-occurring cannabis dependence and depressive disorders. *Addiction.* 2013;108(6):1084-1094.
662. Spring B, Doran N, Pagoto S, et al. Fluoxetine, smoking, and history of major depression: a randomized controlled trial. *J Consult Clin Psychol.* 2007;75(1):85-94.
663. Winstanley EL, Bigelow GE, Silverman K, Johnson RE, Strain EC. A randomized controlled trial of fluoxetine in the treatment of cocaine dependence among methadone-maintained patients. *J Subst Abuse Treat.* 2011;40(3):255-64. doi:10.1016/j.jsat.2010.11.010

664. Shoptaw S, Huber A, Peck J, et al. Randomized, placebo-controlled trial of sertraline and contingency management for the treatment of methamphetamine dependence *Drug Alcohol Depend.* 2006;85(12-18)
665. LeMarquand D, Pihl RO, Benkelfat C. Serotonin and alcohol intake, abuse, and dependence: clinical evidence. *Biol Psychiatry.* 1994;36(5):326-337.
666. McHugh RK, Hofmann SG, Asnaani A, Sawyer AT, Otto MW. The serotonin transporter gene and risk for alcohol dependence: a meta-analytic review. *Drug Alcohol Depend.* 2010;108(1-2):1-6.
667. Kranzler HR, Armeli S, Tennen H, Covault J. 5-HTTLPR genotype and daily negative mood moderate the effects of sertraline on drinking intensity. *Addict Behav.* 2013;18(6):1024-1031.
668. Brookwell L, Hogan C, Healy D, Mangin D. Ninety-three cases of alcohol dependence following SSRI treatment. *Int J Risk Saf Med.* 2014;26(2):99-107.
669. Atigari OV, Kelly AM, Jabeen Q, Healy D. New onset alcohol dependence linked to treatment with selective serotonin reuptake inhibitors. *Int J Risk Saf Med.* 2013;25(2):105-109.
670. Zorick T, Sugar CA, Helleman G, Shoptaw S, London ED. Poor response to sertraline in methamphetamine dependence is associated with sustained craving for methamphetamine *Drug Alcohol Depend.* 2011;118:500-503.
671. Kelly MA, M P, Glass A, et al. Do withdrawal-like symptoms mediate increased marijuana smoking in individuals treated with venlafaxine-XR? *Drug Alcohol Depend.* 2014;144:42-46.
672. Ebrahim S, Bance S, Athale A, Malachowski C, Ioannidis JP. Meta-analyses with industry involvement are massively published and report no caveats for antidepressants. *J Clin Epidemiol.* 2016;70:155-63. doi:10.1016/j.jclinepi.2015.08.021
673. Kishi T, Sevy S, Chekuri R, Correll CU. Antipsychotics for primary alcohol dependence: a Systematic review and meta-analysis of placebo-controlled trials. *J Clin Psychiatry.* 2013;74(7)
674. Wiesbeck GA, Weijers HG, Lesch OM, Glaser T, Toennes PJ, Boening J. Flupenthixol decanoate and relapse prevention in alcoholics: results from a placebo-controlled study. *Alcohol Alcohol.* 2001;36(4):329-334.
675. Guardia J, Segura L, Gonzalvo B, et al. A double-blind, placebo-controlled study of olanzapine in the treatment of alcohol-dependence disorder. *Alcohol Clin Exp Res.* 2004;28(5):736-745.
676. Litten RZ, Fertig JB, Falk DE, et al. A double-blind, placebo-controlled trial to assess the efficacy of quetiapine fumarate XR in very heavy-drinking alcohol-dependent patients. *Alcohol Clin Exp Res.* 2021;36(3):406-416.
677. Martinotti G, Di Nicola M, Di Giannantonio M, Janiri L. Aripiprazole in the treatment of patients with alcohol dependence: a double-blind, comparison trial vs. naltrexone. *J Psychopharmacol (Oxf).* 2009;23(2):123-129. doi:<https://dx.doi.org/10.1177/0269881108089596>
678. Brown ES, Garza M, Carmody TJ. A randomized, double-blind, placebo-controlled add-on trial of quetiapine in outpatients with bipolar disorder and alcohol use disorders. *J Clin Psychiatry.* 2008;69(5):701-705.



679. Kampman KM, Pettinati H, Lynch KG, Sparkman T, O'Brien CP. A pilot trial of olanzapine for the treatment of cocaine dependence. *Drug Alcohol Depend.* 2003;70:265-273.
680. Samaha AN. Can antipsychotic treatment contribute to drug addiction in schizophrenia? *Prog Neuropsychopharmacol Biol Psychiatry.* 2014;52:9-16. doi:10.1016/j.pnpbp.2013.06.008
681. Cooper ZD, Foltin RW, Hart CL, Vosburg SK, Comer SD, Haney M. A human laboratory study investigating the effects of quetiapine on marijuana withdrawal and relapse in daily marijuana smokers. *Addict Biol.* 2013;18(6):993-1002.
682. Dawe S, Gerada C, Russell MA, Gray JA. Nicotine intake in smokers increases following a single dose of haloperidol. *Psychopharmacol.* 1995;117(1):110-115.
683. Whitton AE, Green AI, Pizzagalli DA, Roth RM, Williams JM, Brunette MF. Potent dopamine D2 antagonist block the reward-enhancing effects of nicotine in smokers with schizophrenia. *Schizophr Bull.* 2019;45(6):1300-1308.
684. Haney M, Rubin E, Foltin RW. Aripiprazole maintenance increases smoked cocaine self-administration in humans. *Psychopharmacology (Berl).* 2011;216(3):379-387.
685. Tiihonen J, Kuoppasalmi K, Föhr J, et al. A comparison of aripiprazole, methylphenidate, and placebo for amphetamine dependence. *Am J Psychiatry.* 2007;164(1):160-162.
686. Voronin K, Randall P, Myrick H, Anton R. Aripiprazole effects on alcohol consumption and subjective reports in a clinical laboratory paradigm--possible influence of self-control. *Alcoholism: Clinical & Experimental Research.* 2008;32(11):1954-1961. doi:<https://dx.doi.org/10.1111/j.1530-0277.2008.00783.x>
687. Anton RF, Schacht JP, Voronin KE, Randall PK. Aripiprazole Suppression of Drinking in a Clinical Laboratory Paradigm: Influence of Impulsivity and Self-Control. *Alcoholism: Clinical & Experimental Research.* 2017;41(7):1370-1380. doi:<https://dx.doi.org/10.1111/acer.13417>
688. Gao K, Ganocy SJ, Conroy C, Brownrigg B, Serrano MB, Calabrese JR. A placebo controlled study of quetiapine-XR in bipolar depression accompanied by generalized anxiety with and without a recent history of alcohol and cannabis use. *Psychopharmacology (Berl).* 2017;234(15):2233-2244. doi:<https://dx.doi.org/10.1007/s00213-017-4642-5>
689. Soyka M, Aichmuller C, Bardeleben UV, et al. Flupenthixol in relapse prevention in schizophrenics with comorbid alcoholism: Results from an open clinical study. *Eur Addict Res.* 2003;9(2):65-72. doi:<http://dx.doi.org/10.1159/000068809>
690. Martinotti G, Andreoli S, Di Nicola M, Di Giannantonio M, Sarchiapone M, Janiri L. Quetiapine decreases alcohol consumption, craving, and psychiatric symptoms in dually diagnosed alcoholics. *Hum Psychopharmacol.* 2008;23(5):417-424. doi:<https://dx.doi.org/10.1002/hup.944>
691. Hutchison KE, Swift R, Rohsenow DJ, Monti PM, Davidson D, Almeida A. Olanzapine reduces urge to drink after drinking cues and a priming dose of alcohol. *Psychopharmacology (Berl).* 2001;155(1):27-34.

692. Hutchison KE, Wooden A, Swift RM, et al. Olanzapine reduces craving for alcohol: a DRD4 VNTR polymorphism by pharmacotherapy interaction. *Neuropsychopharmacology*. 2003;28(10):1882-1888.
693. Moallem N, Ray LA. Quetiapine improves response inhibition in alcohol dependent patients: a placebo-controlled pilot study. *Pharmacology, Biochemistry & Behavior*. 2012;100(3):490-493. doi:<https://dx.doi.org/10.1016/j.pbb.2011.10.012>
694. Haass-Koffler CL, Goodyear K, Zywiak WH, Leggio L, Kenna GA, Swift RM. Comparing and Combining Topiramate and Aripiprazole on Alcohol-Related Outcomes in a Human Laboratory Study. *Alcohol Alcohol*. 2018;53(3):268-276. doi:10.1093/alcalc/agx108
695. Solmi M, Murru A, Pacchiarotti I, et al. Safety, tolerability, and risks associated with first- and second-generation antipsychotics: a state-of-the-art clinical review. *Therapeutics and Clinical Risk Management*. 2017;13:757-777. doi:10.2147/TCRM.S117321
696. Pisani F, Oteri G, Costa C, Di Raimondo G, Di Perri R. Effects of Psychotropic Drugs on Seizure Threshold. *Drug Saf*. 2002;25(2):91-110. doi:10.2165/00002018-200225020-00004
697. Koski A, Ojanpera I, Vuori E. Alcohol and benzodiazepines in fatal poisonings. *Alcohol Clin Exp Res*. 2002;26(7):956-959. doi:10.1097/01.alc.0000021337.78063.67
698. Woods JH, Katz JL, Winger G. Abuse liability of benzodiazepines. Review. *Pharmacol Rev*. 1987;39(4):251-413.
699. Woods JH, Katz JL, Winger G. Benzodiazepines - use, abuse, and consequences. Review. *Pharmacol Rev*. 1992;44(2):151-347.
700. Hojer J, Baehrendtz S, Gustafsson L. Benzodiazepine poisoning - experience of 702 admissions to an intensive-care unit during a 14-year period. *J Intern Med*. 1989;226(2):117-122.
701. Stenbacka M, Jansson B, Leifman A, Romelsjo A. Association between use of sedatives or hypnotics, alcohol consumption, or other risk factors and a single injurious fall or multiple injurious falls: a longitudinal general population study. *Alcohol*. 2002;28(1):9-16. Pii s0741-8329(02)00223-9. doi:10.1016/s0741-8329(02)00223-9
702. Poulos CX, Zack M. Low-dose diazepam primes motivation for alcohol and alcohol-related semantic networks in problem drinkers *Behav Pharmacol*. 2004;15(7):503-512.
703. Reif S, Braude L, Lyman DR, et al. Peer Recovery Support for Individuals With Substance Use Disorders: Assessing the Evidence. *Psych Serv*. 2014;65(7):853-861. doi:10.1176/appi.ps.201400047
704. Bassuk EL, Hanson J, Greene RN, Richard M, Laudet A. Peer-Delivered Recovery Support Services for Addictions in the United States: A Systematic Review. Review. *J Subst Abuse Treat*. 2016;63:1-9. doi:10.1016/j.jsat.2016.01.003
705. Best D, Turning Point, Easternhealth, South Pacific Private. *The Australian Life in Recovery Survey*. 2015. Accessed May 23, 2023. [https://www.rec-path.co.uk/wp-content/uploads/2017/10/2015\\_au\\_life\\_in\\_recovery\\_survey.pdf](https://www.rec-path.co.uk/wp-content/uploads/2017/10/2015_au_life_in_recovery_survey.pdf)

706. McQuaid R, Aqsa M, Moussouni K, et al. *Life in Recovery from Addiction in Canada: Technical Report*. 2017. Accessed April 7, 2020. <http://www.ccsa.ca/Resource%20Library/CCSA-Life-in-Recovery-from-Addiction-Report-2017-en.pdf>
707. Laudet AB. *Life in Recovery: Report on the Survey Findings*. Faces & Voices of Recovery; 2013. April 7, 2020. <https://facesandvoicesofrecovery.org/wp-content/uploads/2019/06/22Life-in-Recovery22-Report-on-the-Survey-Findings.pdf>
708. Best DW, Albertson K, Irving J, et al. *UK Life in Recovery Survey 2015: The first national UK survey of addiction recovery experiences*. 2015. Accessed April 7, 2020. <http://www.drugsandalcohol.ie/24542/1/UK%20Life%20in%20Recovery%20FINAL%20-%20222915.pdf>
709. Project MATCH (Matching Alcoholism Treatment to Client Heterogeneity): rationale and methods for a multisite clinical trial matching patients to alcoholism treatment. *Alcohol Clin Exp Res*. 1993;17(6):1130-45.
710. Ferri M, Amato L, Davoli M. Alcoholics Anonymous and other 12-step programmes for alcohol dependence. *Cochrane Database Syst Rev*. 2006;(3)Cd005032. doi:10.1002/14651858.CD005032.pub2
711. Kelly JF, Humphreys K, Ferri M. Alcoholics Anonymous and other 12-step programs for alcohol use disorder. *Cochrane Database Syst Rev*. 2020;3:CD012880. doi:<https://dx.doi.org/10.1002/14651858.CD012880.pub2>
712. Rice SL, Tonigan JS. Impressions of Alcoholics Anonymous (AA) Group Cohesion: A Case for a Nonspecific Factor Predicting Later AA Attendance. *Alcohol Treat Q*. 2012;30(1):40-51. doi:10.1080/07347324.2012.635550
713. Kelly JF, Hoepfner B, Stout RL, Pagano M. Determining the relative importance of the mechanisms of behavior change within Alcoholics Anonymous: a multiple mediator analysis. *Addiction*. 2012;107(2):289-299. doi:10.1111/j.1360-0443.2011.03593.x
714. Moos RH. Active ingredients of substance use-focused self-help groups. *Addiction*. 2008;103(3):387-396. doi:10.1111/j.1360-0443.2007.02111.x
715. Laudet A. The Road to Recovery: Where Are We Going and How Do We Get There? Empirically Driven Conclusions and Future Directions for Service Development and Research. *Subst Use Misuse*. 2008;43(12-13):2001-2020. Pii 905630962. doi:10.1080/10826080802293459
716. Nace EP. Chapter 69: Twelve-Step Programs in Addiction Recovery. In: Ries RK, Fiellin DA, Miller SC, Saitz R, eds. *The ASAM Principles of Addiction Medicine*. 5th ed. Wolters Kluwer Health; 2014:1033-1042.
717. Ranes B, Johnson R, Nelson L, Slaymaker V. The Role of Spirituality in Treatment Outcomes Following a Residential 12-Step Program. *Alcohol Treat Q*. 2017;35(1):16-33. doi:10.1080/07347324.2016.1257275
718. Dermatis H, Galanter M. The Role of Twelve-Step-Related Spirituality in Addiction Recovery. *J Relig Health*. 2016;55(2):510-521. doi:10.1007/s10943-015-0019-4
719. Atkins RG, Hawdon JE. Religiosity and participation in mutual-aid support groups for addiction. *J Subst Abuse Treat*. 2007;33(3):321-31. doi:10.1016/j.jsat.2007.07.001

720. Wild TC. Compulsory substance-user treatment and harm reduction: a critical analysis. *Subst Use Misuse*. 1999;34(1):83-102.
721. Klag S, O'Callaghan F, Creed P. The use of legal coercion in the treatment of substance abusers: an overview and critical analysis of thirty years of research. *Subst Use Misuse*. 2005;40(12):1777-95.
722. Urbanoski KA. Coerced addiction treatment: Client perspectives and the implications of their neglect. *Harm Reduct J*. 2010;7:1-10. 13. doi:10.1186/1477-7517-7-13
723. Horvath AT, Yeterian J. SMART Recovery: Self-Empowering, Science-Based Addiction Recovery Support. *J Groups Addict Recovery*. 2012;7(2-4):102-117.
724. Beck AK, Forbes E, Baker AL, et al. Systematic Review of SMART Recovery: Outcomes, Process Variables, and Implications for Research. *Psychol Addict Behav*. 2017;31(1):1-20. doi:10.1037/adb0000237
725. Hester RK, Lenberg KL, Campbell W, Delaney HD. Overcoming Addictions, a Web-Based Application, and SMART Recovery, an Online and In-Person Mutual Help Group for Problem Drinkers, Part 1: Three-Month Outcomes of a Randomized Controlled Trial. *J Med Internet Res*. 2013;15(7):45-59. UNSP e134. doi:10.2196/jmir.2565
726. Timko C, Sutkowi A, Cronkite RC, Makin-Byrd K, Moos RH. Intensive referral to 12-step dual-focused mutual-help groups. *Drug Alcohol Depend*. 2011;118(2-3):194-201. doi:10.1016/j.drugalcdep.2011.03.019
727. Vederhus JK, Timko C, Kristensen O, Hjemdahl B, Clausen T. Motivational intervention to enhance post-detoxification 12-Step group affiliation: a randomized controlled trial. *Addiction*. 2014;109(5):766-773. doi:10.1111/add.12471
728. Grant K, Young LB, Tyler KA, Simpson JL, Pulido RD, Timko C. Intensive referral to mutual-help groups: A field trial of adaptations for rural veterans. *Patient Educ Couns*. 2018;101(1):79-84. doi:10.1016/j.pec.2017.07.012
729. Manning V, Best D, Faulkner N, et al. Does active referral by a doctor or 12-Step peer improve 12-Step meeting attendance? Results from a pilot randomised control trial. *Drug Alcohol Depend*. 2012;126(1-2):131-137. doi:10.1016/j.drugalcdep.2012.05.004
730. Plattor C. *Many Roads, One Journey: Moving Beyond the 12 Steps*. Harper-Collins; 1992.
731. Valeri L, Sugarman DE, Reilly ME, McHugh RK, Fitzmaurice GM, Greenfield SF. Group therapy for women with substance use disorders: In-session affiliation predicts women's substance use treatment outcomes. *J Subst Abuse Treat*. 2018;94:60-68. doi:<http://dx.doi.org/10.1016/j.jsat.2018.08.008>
732. Tracy K, Wallace SP. Benefits of peer support groups in the treatment of addiction. *Subst Abuse Rehab*. 2016;7:143-154. doi:10.2147/sar.s81535
733. Guldish J, Werdegar D, Sorensen JL, Clark W, Acampora A. Drug abuse day treatment: A randomized clinical trial comparing day and residential treatment programs. *J Consult Clin Psych*. 1998;66(2):280-289. doi:10.1037/0022-006x.66.2.280

734. Rychtarik RG, Connors GJ, Whitney RB, McGillicuddy NB, Fitterling JM, Wirtz PW. Treatment settings for persons with alcoholism: Evidence for matching clients to inpatient versus outpatient care. *J Consult Clin Psych.* 2000;68(2):277-289. doi:10.1037//0022-006x.68.2.277
735. McKay JR, Alterman AI, McLellan AT, Snider EC, Obrien CP. Effect of random versus nonrandom assignment in a comparison of inpatient and day hospital rehabilitation for male alcoholics. *J Consult Clin Psych.* 1995;63(1):70-78. doi:10.1037/0022-006x.63.1.70
736. Reif S, George P, Braude L, et al. Residential Treatment for Individuals With Substance Use Disorders: Assessing the Evidence. *Psych Serv.* 2014;65(3):301-312. doi:10.1176/appi.ps.201300242
737. Finney JW, Hahn AC, Moos RH. The effectiveness of inpatient and outpatient treatment for alcohol abuse: The need to focus on mediators and moderators of setting effects. *Addiction.* 1996;91(12):1773-1796. doi:10.1111/j.1360-0443.1996.tb03801.x
738. McCarty D, Braude L, Lyman DR, et al. Substance abuse intensive outpatient programs: assessing the evidence. *Psychiatr Serv.* 2014;65(6):718-726. doi:10.1176/appi.ps.201300249
739. Harrison PA, Asche SE. Comparison of substance abuse treatment outcomes for inpatients and outpatients. *J Subst Abuse Treat.* 1999;17(3):207-220. doi:10.1016/s0740-5472(99)00004-5
740. de Andrade D, Elphinston RA, Quinn C, Allan J, Hides L. The effectiveness of residential treatment services for individuals with substance use disorders: A systematic review. *Drug Alcohol Depend.* 2019;201:227-235. doi:10.1016/j.drugalcdep.2019.03.031
741. Finney JW MR, Wilbourne PL., Chapter 26: Effects of treatment setting, duration, and amount on patient outcomes. In: Ries RK, Fiellin DA, Miller SC, Saitz R, eds. *The ASAM Principles of Addiction Medicine.* 5th ed. Wolters Kluwer Health; 2014.
742. Smith LA, Gates S, Foxcroft D. Therapeutic communities for substance related disorder. *Cochrane Database Syst Rev.* 2006;(1)Cd005338. doi:10.1002/14651858.CD005338.pub2
743. Tuten M, DeFulio A, Jones HE, Stitzer M. Abstinence-contingent recovery housing and reinforcement-based treatment following opioid detoxification. *Addiction.* 2012;107(5):973-982. doi:10.1111/j.1360-0443.2011.03750.x
744. Jason LA, Olson BD, Ferrari JR, Majer JM, Alvarez J, Stout J. An examination of main and interactive effects of substance abuse recovery housing on multiple indicators of adjustment. *Addiction.* 2007;102(7):1114-1121. doi:10.1111/j.1360-0443.2007.01846.x
745. Reif S, George P, Braude L, et al. Recovery Housing: Assessing the Evidence. Article. *Psych Serv.* 2014;65(3):295-300. doi:10.1176/appi.ps.201300243
746. Rog DJ, Marshall T, Dougherty RH, et al. Permanent Supportive Housing: Assessing the Evidence. *Psych Serv.* 2014;65(3):287-294. doi:10.1176/appi.ps.201300261
747. Hser YI, Polinsky ML, Maglione M, Anglin MD. Matching clients' needs with drug treatment services. *J Subst Abuse Treat.* 1999;16(4):299-305. doi:10.1016/s0740-5472(98)00037-3

748. Penzenstadler L, Machado A, Thorens G, Zullino D, Khazaal Y. Effect of Case Management Interventions for Patients with Substance Use Disorders. *Front Psychiatr*. 2017;851. doi:10.3389/fpsy.2017.00051
749. Simoneau H, Kamgang E, Tremblay J, Bertrand K, Brochu S, Fleury MJ. Efficacy of extensive intervention models for substance use disorders: A systematic review. *Drug Alcohol Rev*. 2018;37(Suppl 1):S246-S262. doi:10.1111/dar.12590
750. Drummond C, Gilbert H, Burns T, et al. Assertive Community Treatment For People With Alcohol Dependence: A Pilot Randomized Controlled Trial. *Alcohol Alcohol*. 2017;52(2):234-241. doi:10.1093/alcalc/agn091
751. Passeti F, Jones G, Chawla K, Boland B, Drummond C. Pilot study of assertive community treatment methods to engage alcohol-dependent individuals. *Alcohol Alcohol*. 2008;43(4):451-455. doi:10.1093/alcalc/agn025
752. Statistics Canada. Indigenous population continues to grow and is much younger than the non-Indigenous population, although the pace of growth has slowed. Accessed October 27, 2022. <https://www150.statcan.gc.ca/n1/daily-quotidien/220921/dq220921a-eng.htm>
753. Statistics Canada. *The Daily – Aboriginal peoples in Canada: Key results from the 2016 Census*. 2017. Published October 25, 2017. Accessed April 7, 2020. <https://www150.statcan.gc.ca/n1/daily-quotidien/171025/dq171025a-eng.htm>
754. Paradies Y. A systematic review of empirical research on self-reported racism and health. *Int J Epidemiol*. 2006;35(4):888-901. doi:10.1093/ije/dyl056
755. Brave Heart MY. The historical trauma response among natives and its relationship with substance abuse: a Lakota illustration. *J Psychoactive Drugs*. 2003;35(1):7-13. doi:10.1080/02791072.2003.10399988
756. Statistics Canada. *Table 13-10-0099-01 – Health indicator profile, by Aboriginal identity and sex, age-standardized rate, four year estimates (2007-2014)*. 2016. Published February 2, 2019. Accessed October 27, 2022. <https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1310009901>
757. Marsh TN, Cote-Meek S, Young NL, Najavits LM, Toulouse P. Indigenous Healing and Seeking Safety: A Blended Implementation Project for Intergenerational Trauma and Substance Use Disorders. *Int Indigenous Policy J*. 2016;7(2)Unsp 3. doi:10.18584/iipj.2016.7.2.3
758. Ellerby JH, McKenzie J, McKay S, Garipey GJ, Kaufert JM. Bioethics for clinicians: 18. Aboriginal cultures. *CMAJ*. 2000;163(7):845-50.
759. Freedman B. Offering truth. One ethical approach to the uninformed cancer patient. *Arch Intern Med*. 1993;153(5):572-6.
760. Rowan M, Poole N, Shea B, et al. Cultural interventions to treat addictions in Indigenous populations: findings from a scoping study. *Subst Abuse Treat Prev Policy*. 2014;9:34. doi:10.1186/1747-597X-9-34
761. Thomas LR, Donovan DM, Sigo RL, Austin L, Marlatt GA, Suquamish Tribe. The Community Pulling Together: A Tribal Community-University Partnership Project to Reduce Substance Abuse and Promote Good Health in a Reservation Tribal Community. *J Ethn Subst Abuse*. 2009;8(3):283-300. doi:10.1080/15332640903110476

762. Rowan M, Poole N, Shea B, et al. A scoping study of cultural interventions to treat addictions in Indigenous populations: methods, strategies and insights from a Two-Eyed Seeing approach. *Subst Abuse Treat Prev Policy*. 2015;10:26. doi:10.1186/s13011-015-0021-6
763. Marsh TN, Marsh DC, Ozawagosh J, Ozawagosh F. The Sweat Lodge Ceremony: A Healing Intervention for Intergenerational Trauma and Substance Use. *Int Indig Policy J*. 2018;9(2)doi:10.18584/iipj.2018.9.2.2
764. Purcell-Khodr GC, Lee KSK, Conigrave JH, Webster E, Conigrave KM. What can primary care services do to help First Nations people with unhealthy alcohol use? A systematic review: Australia, New Zealand, USA and Canada. *Addiction Science & Clinical Practice*. 2020;15(1):31. doi:<https://dx.doi.org/10.1186/s13722-020-00204-8>
765. Auger M, Howell T, Gomes T. Moving toward holistic wellness, empowerment and self-determination for Indigenous peoples in Canada: Can traditional Indigenous health care practices increase ownership over health and health care decisions? *Can J Public Health*. 2016;107(4):e393-e398. doi:10.17269/CJPH.107.5366
766. Truth and Reconciliation Commission of Canada. *Truth and Reconciliation Commission of Canada: Calls to Action*. 2015. <http://trc.ca/assets/pdf>
767. Provincial Health Services Authority. *Dancing in Both Worlds: a Review of the Aboriginal Patient Liaison/Navigation Program in British Columbia*. 2015. Accessed May 23, 2023. <https://silo.tips/download/dancing-in-both-worlds>
768. Aboriginal Health VCH. *Aboriginal Cultural Practices: A Guide For Physicians and Allied Health Care Professionals Working at Vancouver Coastal Health*. <http://www.vch.ca/Documents/AH-cultural-practices.pdf>
769. World Health Organization (WHO), Pan American Health Organization (PAHO). *Gender, Health and Alcohol Use*. WHO. Published September 2005. Accessed May 23, 2023. <https://www.who.int/publications/m/item/gender-health-and-alcohol-use>
770. National Alcohol Strategy Advisory Committee. *Low-Risk Drinking Guideline Summary: Women and Alcohol*. Canadian Centre on Substance Use and Addiction (CCSA); 2014. Accessed April 7, 2020. <https://www.ccsa.ca/sites/default/files/2019-05/CCSA-Women-and-Alcohol-Summary-2014-en.pdf>
771. Kay A, Taylor TE, Barthwell AG, Wichelecki J, Leopold V. Substance Use and Women's Health. *J Addict Dis*. 2010;29(2):139-163.
772. Rehm J, Taylor B, Mohapatra S, et al. Alcohol as a risk factor for liver cirrhosis: A systematic review and meta-analysis. *Drug Alcohol Rev*. 2010;29(4):437-445.
773. Chen P, Jacobson KC. Developmental Trajectories of Substance Use From Early Adolescence to Young Adulthood: Gender and Racial/Ethnic Differences. *J Adolesc Health*. 2012;50(2):154-163. doi:<https://doi.org/10.1016/j.jadohealth.2011.05.013>
774. Nock MK, Kazdin AE, Hiripi E, Kessler RC. Prevalence, subtypes, and correlates of DSM-IV conduct disorder in the National Comorbidity Survey Replication. *Psych Med*. 2006;36(5):699-710.
775. Nolen-Hoeksema S. Gender differences in risk factors and consequences for alcohol use and problems. *Clin Psych Rev*. 2004;24(8):981-1010.

776. Uy PJ, Massoth NA, Gottdiener WH. Rethinking male drinking: Traditional masculine ideologies, gender-role conflict, and drinking motives. *Psych Men Masc*. 2014;15(2):121.
777. Scheim AI, Bauer GR, Shokoohi M. Heavy episodic drinking among transgender persons: Disparities and predictors. *Drug Alcohol Depend*. 2016;167:156-62. doi:10.1016/j.drugalcdep.2016.08.011
778. DeMartini KS, Carey KB, Lao K, Luciano M. Injunctive norms for alcohol-related consequences and protective behavioral strategies: Effects of gender and year in school. *Addict Behav*. 2011;36(4):347-353. doi:<https://doi.org/10.1016/j.addbeh.2010.12.009>
779. Myers B, Carney T, Wechsberg WM. "Not on the agenda": A qualitative study of influences on health services use among poor young women who use drugs in Cape Town, South Africa. *Int J Drug Policy*. 2016;30(Supplement C):52-58. doi:<https://doi.org/10.1016/j.drugpo.2015.12.019>
780. Bazargan-Hejazi S, De Lucia V, Pan D, et al. Gender Comparison in Referrals and Treatment Completion to Residential and Outpatient Alcohol Treatment. *Subst Abus Res Treat*. 2016;10:SART.S39943. doi:10.4137/sart.s39943
781. Nathoo T, Poole N, Wolfson L, Schmidt R, Hemsing N, Gelb K. *Doorways to Conversation: Brief Intervention on Substance Use with Girls and Women*. Centre of Excellence in Women's Health; 2018. Accessed April 7, 2020. [http://bccwh.bc.ca/wp-content/uploads/2018/06/Doorways\\_ENGLISH\\_July-18-2018\\_online-version.pdf](http://bccwh.bc.ca/wp-content/uploads/2018/06/Doorways_ENGLISH_July-18-2018_online-version.pdf)
782. Stone R. Pregnant women and substance use: fear, stigma, and barriers to care. *Health Justice*. 2015;3:2. doi:10.1186/s40352-015-0015-5
783. McCaul ME, Roach D, Hasin DS, Weisner C, Chang G, Sinha R. Alcohol and Women: A Brief Overview. *Alcohol Clin Exp Res*. 2019;43(5):774-779. doi:10.1111/acer.13985
784. Gilbert PA, Pass LE, Keuroghlian AS, Greenfield TK, Reisner SL. Alcohol research with transgender populations: A systematic review and recommendations to strengthen future studies. *Drug Alcohol Depend*. 2018;186:138-146. doi:10.1016/j.drugalcdep.2018.01.016
785. Talley AE, Gilbert PA, Mitchell J, Goldbach J, Marshall BDL, Kaysen D. Addressing gaps on risk and resilience factors for alcohol use outcomes in sexual and gender minority populations. *Drug Alcohol Rev*. 2016;35(4):484-493. doi:10.1111/dar.12387
786. Marshall BD, Wood E, Shoveller JA, Patterson TL, Montaner JS, Kerr T. Pathways to HIV risk and vulnerability among lesbian, gay, bisexual, and transgendered methamphetamine users: a multi-cohort gender-based analysis. journal article. *BMC Public Health*. 2011;11(1):20. doi:10.1186/1471-2458-11-20
787. Cochran BN, Stewart AJ, Ginzler JA, Cauce AM. Challenges Faced by Homeless Sexual Minorities: Comparison of Gay, Lesbian, Bisexual, and Transgender Homeless Adolescents With Their Heterosexual Counterparts. *Am J Public Health*. 2002;92(5):773-777.
788. Balsam KF, Huang B, Fieland KC, Simoni JM, Walters KL. Culture, trauma, and wellness: a comparison of heterosexual and lesbian, gay, bisexual, and two-spirit native americans. *Cultur Divers Ethnic Minor Psychol*. 2004;10(3):287-301. doi:10.1037/1099-9809.10.3.287



789. Nathoo T, Poole N, Wolfson L, Schmidt R, Hemsing N, Gelb K. *Doorways to Conversation: Brief Intervention on Substance Use with Girls and Women*. 2018. June. [http://bccewh.bc.ca/wp-content/uploads/2018/06/Doorways\\_ENGLISH\\_July-18-2018\\_online-version.pdf](http://bccewh.bc.ca/wp-content/uploads/2018/06/Doorways_ENGLISH_July-18-2018_online-version.pdf)
790. Flentje A, Heck NC, Sorensen JL. Characteristics of transgender individuals entering substance abuse treatment. *Addict Behav*. 2014;39(5):969-975. doi:10.1016/j.addbeh.2014.01.011
791. Flentje A, Livingston NA, Roley J, Sorensen JL. Mental and Physical Health Needs of Lesbian, Gay, and Bisexual Clients in Substance Abuse Treatment. *J Subst Abuse Treat*. 2015;58:78-83. doi:10.1016/j.jsat.2015.06.022
792. Fish JN, Hughes TL, Russell ST. Sexual identity differences in high-intensity binge drinking: findings from a US national sample. *Addiction*. 2018;113(4):749-758. doi:10.1111/add.14041
793. Schuler MS, Rice CE, Evans-Polce RJ, Collins RL. Disparities in substance use behaviors and disorders among adult sexual minorities by age, gender, and sexual identity. *Drug Alcohol Depend*. 2018;189:139-146. doi:10.1016/j.drugalcdep.2018.05.008
794. Trinh MH, Agenor M, Austin SB, Jackson CL. Health and healthcare disparities among US women and men at the intersection of sexual orientation and race/ethnicity: a nationally representative cross-sectional study. *BMC Public Health*. 2017;17(1):964. 964. doi:10.1186/s12889-017-4937-9
795. Fish JN, Baams L. Trends in Alcohol-Related Disparities Between Heterosexual and Sexual Minority Youth from 2007 to 2015: Findings from the Youth Risk Behavior Survey. *LGBT Health*. 2018;5(6):359-367. doi:10.1089/lgbt.2017.0212
796. Coulter RWS, Bersamin M, Russell ST, Mair C. The Effects of Gender- and Sexuality-Based Harassment on Lesbian, Gay, Bisexual, and Transgender Substance Use Disparities. *J Adolesc Health*. 2018;62(6):688-700. doi:10.1016/j.jadohealth.2017.10.004
797. Hughto JMW, Quinn EK, Dunbar MS, Rose AJ, Shireman TI, Jasuja GK. Prevalence and Co-occurrence of Alcohol, Nicotine, and Other Substance Use Disorder Diagnoses Among US Transgender and Cisgender Adults. *JAMA Network Open*. 2021;4(2):e2036512-e2036512. doi:10.1001/jamanetworkopen.2020.36512
798. White Hughto JM, Pachankis JE, Willie TC, Reisner SL. Victimization and depressive symptomology in transgender adults: The mediating role of avoidant coping. *J Couns Psychol*. 2017;64(1):41-51. doi:10.1037/cou0000184
799. Reisner SL, Pardo ST, Gamarel KE, White Hughto JM, Pardee DJ, Keo-Meier CL. Substance Use to Cope with Stigma in Healthcare Among U.S. Female-to-Male Trans Masculine Adults. *LGBT Health*. 2015;2(4):324-32. doi:10.1089/lgbt.2015.0001
800. Cochran BN, Cauce AM. Characteristics of lesbian, gay, bisexual, and transgender individuals entering substance abuse treatment. *J Subst Abuse Treat*. 2006;30(2):135-146. doi:<https://doi.org/10.1016/j.jsat.2005.11.009>
801. Hunt J. *Why the Gay and Transgender Population Experiences Higher Rates of Substance Use*. 2012. March 9, 2012. Accessed April 23, 2023. <https://www.americanprogress.org/article/why-the-gay-and-transgender-population-experiences-higher-rates-of-substance-use/>

802. MULLENS AB, YOUNG RM, DUNNE MP, NORTON G. The Drinking Expectancy Questionnaire for Men who have Sex with Men (DEQ-MSM): A measure of substance-related beliefs. *Drug and Alcohol Review*. 2011;30(4):372-380. doi:<https://doi.org/10.1111/j.1465-3362.2010.00225.x>
803. A Provider's Introduction to Substance Abuse Treatment for Lesbian, Gay, Bisexual, and Transgender Individuals (Substance Abuse and Mental Health Services Administration) (2012).
804. Vries A, Cohen-Kettenis P, Henriette D-V, Waal D, White Holman C, Goldberg J. *Caring for Transgender Adolescents in BC: Suggested Guidelines Clinical Management of Gender Dysphoria in Adolescents Ethical, Legal, and Psychosocial Issues in Care of Transgender Adolescents*. 2006.
805. Health S. *Guidelines for gender-affirming primary care with trans and non-binary patients*. 2021. Accessed November 8, 2022. <https://rainbowhealth.wpenginepowered.com/wp-content/uploads/2021/06/Guidelines-FINAL-4TH-EDITION-c.pdf>
806. Bekkering GE, Aertgeerts B, Asueta-Lorente JF, et al. Practitioner review: evidence-based practice guidelines on alcohol and drug misuse among adolescents: a systematic review. *J Child Psych Psych Allied Disc*. 2014;55(1):3-21. doi:<https://dx.doi.org/10.1111/jcpp.12145>
807. Levy S, Williams JF. Adolescent substance use: the role of the medical home. *Adolesc Med*. 2014;25(1):1-14.
808. Wu LT, Ringwalt CL. Use of alcohol treatment and mental health services among adolescents with alcohol use disorders. *Psychiatr Serv*. 2006;57(1):84-92. doi:10.1176/appi.ps.57.1.84
809. Chun TH, Linakis JG. Interventions for adolescent alcohol use. *Curr Opin Pediatr*. 2012;24(2):238-242. doi:<https://dx.doi.org/10.1097/MOP.0b013e32834faa83>
810. Deas D. Evidence-based treatments for alcohol use disorders in adolescents. *Pediatrics*. 2008;121(Suppl4):S348-S354. doi:10.1542/peds.2007-2243G
811. Hammond CJ, Gray KM. Pharmacotherapy for Substance Use Disorders in Youths. *J Child Adolesc Subst Abuse*. 2016;25(4):292-316. doi:10.1080/1067828X.2015.1037517
812. Slemon A, Jenkins EK, Haines-Saah RJ, Daly Z, Jiao S. "You can't chain a dog to a porch": a multisite qualitative analysis of youth narratives of parental approaches to substance use. *Harm Reduct J*. 2019;16(1):26. doi:10.1186/s12954-019-0297-3
813. Jenkins EK, Slemon A, Haines-Saah RJ. Developing harm reduction in the context of youth substance use: insights from a multi-site qualitative analysis of young people's harm minimization strategies. *Harm Reduct J*. 2017;14(1):53. doi:10.1186/s12954-017-0180-z
814. Barton J, Hendreson, J. Peer Support and Youth Recovery: A Brief Review of the Theoretical Underpinnings and Evidence. *Can J Fam Youth*. 2016;8(1):1-17.
815. MacArthur GJ, Harrison S, Caldwell DM, Hickman M, Campbell R. Peer-led interventions to prevent tobacco, alcohol and/or drug use among young people aged 11-21years: a systematic review and meta-analysis. *Addiction*. 2016;111(3):391-407. doi:10.1111/add.13224

816. Goodyear T, Jenkins E, Knight R, et al. Autonomy and (In) Capacity to Consent in Adolescent Substance Use Treatment and Care. *J Adolesc Health*. 2022;
817. The Canadian Medical Protective Association. *Duties and responsibilities: Expectations of physicians in practice. Can a child provide consent?* The Canadian Medical Protective Association; 2016. Accessed April 8, 2020. <https://www.cmpa-acpm.ca/en/advice-publications/browse-articles/2014/can-a-child-provide-consent>
818. Jackman M, McRae A, The Royal College of Physicians and Surgeons of Canada (RCPSC). *Medical Decision-Making and Mature Minors*. 2013;1.5.2. Accessed May 23, 2023. <https://ads-uk.org/resources/practice-standards-for-young-people-with-substance-misuse-problems/>
819. Association CMP. *Medico-legal handbook for physicians in Canada*. Updated February 2022. Version 9.0. <https://www.cmpa-acpm.ca/en/advice-publications/handbooks/medical-legal-handbook-for-physicians-in-canada>
820. Public Health Agency of Canada. *What Mothers Say: The Canadian Maternity Experiences Survey*. 2009. Accessed April 8, 2020. <http://www.phac-aspc.gc.ca/rhs-ssg/pdf/survey-eng.pdf>
821. Turner A. *Living arrangements of Aboriginal children aged 14 and under*. 2016. April 13, 2016. <https://oaresource.library.carleton.ca/wcl/2016/20160519/75-006-2016-5-eng.pdf>
822. Ritland L, Thomas V, Jongbloed K, et al. The Cedar Project: Relationship between child apprehension and attempted suicide among young Indigenous mothers impacted by substance use in two Canadian cities. *PLoS ONE*. 2021;16(6):e0252993. doi:10.1371/journal.pone.0252993
823. Allen L, Wodtke L, Hayward A, Read C, Cyr M, Cidro J. Pregnant and early parenting Indigenous women who use substances in Canada: A scoping review of health and social issues, supports, and strategies. *J Ethn Subst Abuse*. 2022;1-31. doi:10.1080/15332640.2022.2043799
824. Shahram SZ, Bottorff JL, Kurtz DL, et al. Understanding the life histories of pregnant-involved young aboriginal women with substance use experiences in three Canadian cities. *Qual Health Res*. 2017;27(2):249-259.
825. Nestor LJ, Murphy A, McGonigle J, et al. Acute naltrexone does not remediate fronto-striatal disturbances in alcoholic and alcoholic polysubstance-dependent populations during a monetary incentive delay task. *Addict Biol*. 2017;22(6):1576-1589. doi:<https://dx.doi.org/10.1111/adb.12444>
826. Khoury JE, Jamieson B, Milligan K. Risk for Childhood Internalizing and Externalizing Behavior Problems in the Context of Prenatal Alcohol Exposure: A Meta-Analysis and Comprehensive Examination of Moderators. Review. *Alcohol Clin Exp Res*. 2018;42(8):1358-1377. doi:10.1111/acer.13805
827. O'Leary CM, Bower C. Guidelines for pregnancy: What's an acceptable risk, and how is the evidence (finally) shaping up? *Drug Alcohol Rev*. 2012;31(2):170-183. doi:10.1111/j.1465-3362.2011.00331.x
828. Statistics Canada. Table 13-10-0096-11 – Heavy drinking, by age group, 2016 and 2017. Published February 9, 2019. Accessed April 3, 2020. <https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1310009611>
829. Rockett IR, Putnam SL, Jia H, Smith GS. Declared and undeclared substance use among emergency department patients: a population-based study. *Addiction*. 2006;101(5):706-12. doi:10.1111/j.1360-0443.2006.01397.x

830. Blazer DG, Wu LT. The epidemiology of at-risk and binge drinking among middle-aged and elderly community adults: National Survey on Drug Use and Health. *Am J Psychiat*. 2009;166(10):1162-9. doi:10.1176/appi.ajp.2009.09010016
831. Aalto M, Alho H, Halme JT, Seppa K. The Alcohol Use Disorders Identification Test (AUDIT) and its derivatives in screening for heavy drinking among the elderly. *Int J Geriatr Psychiatry*. 2011;26(9):881-5. doi:10.1002/gps.2498
832. Caputo F, Vignoli T, Leggio L, Addolorato G, Zoli G, Bernardi M. Alcohol use disorders in the elderly: a brief overview from epidemiology to treatment options. *Exp Gerontol*. 2012;47(6):411-6. doi:10.1016/j.exger.2012.03.019
833. Moore AA, Beck JC, Babor TF, Hays RD, Reuben DB. Beyond alcoholism: identifying older, at-risk drinkers in primary care. *J Stud Alcohol*. 2002;63(3):316-24.
834. Satre DD, Blow FC, Chi FW, Weisner C. Gender differences in seven-year alcohol and drug treatment outcomes among older adults. *Am J Addict*. 2007;16(3):216-21. doi:10.1080/10550490701375673
835. Hunt GE, Large MM, Cleary M, Lai HMX, Saunders JB. Prevalence of comorbid substance use in schizophrenia spectrum disorders in community and clinical settings, 1990-2017: Systematic review and meta-analysis. *Drug Alcohol Depend*. 2018;191:234-258. doi:10.1016/j.drugalcdep.2018.07.011
836. Brown SA, Schuckit MA. Changes in depression among abstinent alcoholics. *Journal of studies on alcohol*. 1988;49(5):412-7.
837. Brown SA, Irwin M, Schuckit MA. Changes in anxiety among abstinent male alcoholics. *Journal of studies on alcohol*. 1991;52(1):55-61.
838. Gossop M, Marsden J, Stewart D. Remission of psychiatric symptoms among drug misusers after drug dependence treatment. *J Nerv Ment Dis*. 2006;194(11):826-32. doi:10.1097/01.nmd.0000244483.17443.0e
839. Mangrum LF. Client and service characteristics associated with addiction treatment completion of clients with co-occurring disorders. *Addict Behav*. 2009;34(10):898-904. doi:10.1016/j.addbeh.2009.03.006
840. Min SY, Whitecraft E, Rothbard AB, Salzer MS. Peer support for persons with co-occurring disorders and community tenure: A survival analysis. *Psychiatr Rehabil J*. 2007;30(3):207-213. doi:10.2975/30.3.2007.207.213
841. Chinman M, George P, Dougherty RH, et al. Peer Support Services for Individuals With Serious Mental Illnesses: Assessing the Evidence. *Psych Serv*. 2014;65(4):429-441. doi:10.1176/appi.ps.201300244
842. John WS, Zhu H, Mannelli P, Schwartz RP, Subramaniam GA, Wu LT. Prevalence, patterns, and correlates of multiple substance use disorders among adult primary care patients. *Drug Alcohol Depend*. 2018;187:79-87. doi:10.1016/j.drugalcdep.2018.01.035
843. Weinberger AH, Funk AP, Goodwin RD. A review of epidemiologic research on smoking behavior among persons with alcohol and illicit substance use disorders. *Prev Med*. 2016;92:148-159. doi:10.1016/j.ypmed.2016.05.011

844. Higgins ST, Kurti AN, Redner R, et al. Co-occurring risk factors for current cigarette smoking in a U.S. nationally representative sample. *Prev Med*. 2016;92:110-117. doi:10.1016/j.ypmed.2016.02.025
845. Smith PH, Mazure CM, McKee SA. Smoking and mental illness in the U.S. population. *Tob Control*. 2014;23(e2):e147-53. doi:10.1136/tobaccocontrol-2013-051466
846. Daeppen JB, Smith TL, Danko GP, et al. Clinical correlates of cigarette smoking and nicotine dependence in alcohol-dependent men and women. The Collaborative Study Group on the Genetics of Alcoholism. *Alcohol Alcohol*. 2000;35(2):171-5.
847. Mason BJ, Leher P. Effects of nicotine and illicit substance use on alcoholism treatment outcomes and acamprosate efficacy. *J Addict Med*. 2009;3(3):164-71. doi:10.1097/ADM.0b013e3181917d53
848. Marrero JA, Fontana RJ, Fu S, Conjeevaram HS, Su GL, Lok AS. Alcohol, tobacco and obesity are synergistic risk factors for hepatocellular carcinoma. *J Hepatol*. 2005;42(2):218-24. doi:10.1016/j.jhep.2004.10.005
849. Pelucchi C, Gallus S, Garavello W, Bosetti C, La Vecchia C. Cancer risk associated with alcohol and tobacco use: focus on upper aero-digestive tract and liver. *Alcohol Res Health*. 2006;29(3):193-8.
850. Durazzo TC, Cardenas VA, Studholme C, Weiner MW, Meyerhoff DJ. Non-treatment-seeking heavy drinkers: effects of chronic cigarette smoking on brain structure. *Drug Alcohol Depend*. 2007;87(1):76-82. doi:10.1016/j.drugalcdep.2006.08.003
851. Ebbert JO, Janney CA, Sellers TA, Folsom AR, Cerhan JR. The association of alcohol consumption with coronary heart disease mortality and cancer incidence varies by smoking history. *J Gen Intern Med*. 2005;20(1):14-20. doi:10.1111/j.1525-1497.2005.40129.x
852. Prochaska JJ, Delucchi K, Hall SM. A meta-analysis of smoking cessation interventions with individuals in substance abuse treatment or recovery. *J Consult Clin Psych*. 2004;72(6):1144-56. doi:10.1037/0022-006x.72.6.1144
853. Weinberger AH, Platt J, Esan H, Galea S, Erlich D, Goodwin RD. Cigarette Smoking Is Associated With Increased Risk of Substance Use Disorder Relapse: A Nationally Representative, Prospective Longitudinal Investigation. *J Clin Psychiatry*. 2017;78(2):e152-e160. doi:10.4088/JCP.15m10062
854. Weinberger AH, Platt J, Jiang B, Goodwin RD. Cigarette Smoking and Risk of Alcohol Use Relapse Among Adults in Recovery from Alcohol Use Disorders. *Alcohol Clin Exp Res*. 2015;39(10):1989-96. doi:10.1111/acer.12840
855. De Soto CB, O'Donnell WE, De Soto JL. Long-term recovery in alcoholics. *Alcohol Clin Exp Res*. 1989;13(5):693-7.
856. Derefinko KJ, Salgado Garcia FI, Sumrok DD. Smoking Cessation for Those Pursuing Recovery from Substance Use Disorders. *Med Clin North Am*. 2018;102(4):781-796. doi:10.1016/j.mcna.2018.02.014
857. Baca CT, Yahne CE. Smoking cessation during substance abuse treatment: what you need to know. *J Subst Abuse Treat*. 2009;36(2):205-19. doi:10.1016/j.jsat.2008.06.003

858. Prochaska JJ. Failure to treat tobacco use in mental health and addiction treatment settings: a form of harm reduction? *Drug Alcohol Depend.* 2010;110(3):177-82. doi:10.1016/j.drugalcdep.2010.03.002
859. Kozlowski LT, Skinner W, Kent C, Pope MA. Prospects for smoking treatment in individuals seeking treatment for alcohol and other drug problems. *Addict Behav.* 1989;14(3):273-8.
860. McClure EA, Acquavita SP, Dunn KE, Stoller KB, Stitzer ML. Characterizing smoking, cessation services, and quit interest across outpatient substance abuse treatment modalities. *J Subst Abuse Treat.* 2014;46(2):194-201. doi:10.1016/j.jsat.2013.07.009
861. Apollonio D, Philipps R, Bero L. Interventions for tobacco use cessation in people in treatment for or recovery from substance use disorders. *Cochrane Database Syst Rev.* 2016;11:Cd010274. doi:10.1002/14651858.CD010274.pub2
862. Minian N, Baliunas D, Zawertailo L, et al. Combining alcohol interventions with tobacco addictions treatment in primary care-the COMBAT study: a pragmatic cluster randomized trial. *Implement Sci.* 2017;12(1):65. doi:10.1186/s13012-017-0595-7
863. Orr MF, Lederhos Smith C, Finlay M, et al. Pilot investigation: randomized-controlled analog trial for alcohol and tobacco smoking co-addiction using contingency management. *Behav Pharmacol.* 2018;29(5):462-468. doi:10.1097/fbp.0000000000000379
864. Yardley MM, Mirbaba MM, Ray LA. Pharmacological Options for Smoking Cessation in Heavy-Drinking Smokers. *CNS Drugs.* 2015;29(10):833-45. doi:10.1007/s40263-015-0284-5
865. Pfizer Canada Inc. Champix (varenicline tartrate tablets) Product Monograph [https://www.pfizer.ca/files/Champix\\_PM\\_221214\\_22Jan2019\\_EN](https://www.pfizer.ca/files/Champix_PM_221214_22Jan2019_EN)
866. Gandhi KD, Mansukhani MP, Karpyak VM, Schneekloth TD, Wang Z, Kolla BP. The Impact of Varenicline on Alcohol Consumption in Subjects With Alcohol Use Disorders: Systematic Review and Meta-Analyses. *J Clin Psychiatry.* 2020;81(2):25. doi:<https://dx.doi.org/10.4088/JCP.19r12924>
867. Oon-Arom A, Likhitsathain S, Srisurapanont M. Efficacy and acceptability of varenicline for alcoholism: A systematic review and meta-analysis of randomized-controlled trials. *Drug & Alcohol Dependence.* 2019;205:107631. doi:<https://dx.doi.org/10.1016/j.drugalcdep.2019.107631>
868. Bold KW, Zweben A, Fucito LM, et al. Longitudinal Findings from a Randomized Clinical Trial of Varenicline for Alcohol Use Disorder with Comorbid Cigarette Smoking. *Alcoholism: Clinical & Experimental Research.* 2019;43(5):937-944. doi:<https://dx.doi.org/10.1111/acer.13994>
869. Falk DE, Castle IJ, Ryan M, Fertig J, Litten RZ. Moderators of Varenicline Treatment Effects in a Double-Blind, Placebo-Controlled Trial for Alcohol Dependence: An Exploratory Analysis. *J Addict Med.* 2015;9(4):296-303. doi:<https://dx.doi.org/10.1097/ADM.0000000000000133>
870. Fucito LM, Wu R, O'Malley SS, et al. An integrated behavioural intervention combined with varenicline for heavy-drinking smokers: A randomized pilot study. *Journal of Smoking Cessation.* 2020;doi:10.1017/jsc.2020.13

871. Jordan CJ, Xi ZX. Discovery and development of varenicline for smoking cessation. *Expert Opin Drug Discov.* 2018;13(7):671-683. doi:10.1080/17460441.2018.1458090
872. Martins SS, Sampson L, Cerda M, Galea S. Worldwide Prevalence and Trends in Unintentional Drug Overdose: A Systematic Review of the Literature. *Am J Public Health.* 2015;105(11):e29-49. doi:10.2105/AJPH.2015.302843
873. Darke S, Zador D. Fatal heroin 'overdose': a review. *Addiction.* 1996;91(12):1765-72.
874. Gossop M, Marsden J, Stewart D, Rolfe A. Patterns of drinking and drinking outcomes among drug misusers 1-year follow-up results. *J Subst Abuse Treat.* 2000;19(1):45-50. doi:10.1016/s0740-5472(99)00097-5
875. Hartzler B, Donovan DM, Huang Z. Comparison of opiate-primary treatment seekers with and without alcohol use disorder. *J Subst Abuse Treat.* 2010;39(2):114-123. doi:10.1016/j.jsat.2010.05.008
876. Ryder N, Cullen W, Barry J, Bury G, Keenan E, Smyth BP. Prevalence of problem alcohol use among patients attending primary care for methadone treatment. *Bmc Family Practice.* 2009;1042. doi:10.1186/1471-2296-10-42
877. Soyka M. Alcohol Use Disorders in Opioid Maintenance Therapy: Prevalence, Clinical Correlates and Treatment. *Eur Addict Res.* 2015;21(2):78-87. doi:10.1159/000363232
878. Kandel DB, Hu MC, Griesler P, Wall M. Increases from 2002 to 2015 in prescription opioid overdose deaths in combination with other substances. *Drug Alcohol Depend.* 2017;178:501-511. doi:10.1016/j.drugalcdep.2017.05.047
879. Leece P, Cavacuiti C, Macdonald EM, et al. Predictors of Opioid-Related Death During Methadone Therapy. *J Subst Abuse Treat.* 2015;57:30-35. doi:10.1016/j.jsat.2015.04.008
880. Witkiewitz K, Vowles KE. Alcohol and Opioid Use, Co-Use, and Chronic Pain in the Context of the Opioid Epidemic: A Critical Review. *Alcohol Clin Exp Res.* 2018;42(3):478-488. doi:10.1111/acer.13594
881. Potter JS, Marino EN, Hillhouse MP, et al. Buprenorphine/Naloxone and Methadone Maintenance Treatment Outcomes for Opioid Analgesic, Heroin, and Combined Users: Findings From Starting Treatment With Agonist Replacement Therapies (START). *Journal of Studies on Alcohol and Drugs.* 2013;74(4):605-613. doi:10.15288/jsad.2013.74.605
882. Rowan-Szal GA, Chatham LR, Simpson DD. Importance of identifying cocaine and alcohol dependent methadone clients. *Am J Addict.* 2000;9(1):38-50.
883. Nolan S, Klimas J, Wood E. Alcohol use in opioid agonist treatment. *Addict Sci Clin Pract.* 2016;11(1):17. doi:10.1186/s13722-016-0065-6
884. Klimas J, Cullen W, Field CA. Problem alcohol use among problem drug users: development and content of clinical guidelines for general practice. Article. *Ir J Med Sci.* 2014;183(1):89-101. doi:10.1007/s11845-013-0982-2

885. Darker CD, Sweeney B, Keenan E, Whiston L, Anderson R, Barry J. Screening and Brief Interventions for Illicit Drug Use and Alcohol Use in Methadone Maintained Opiate-Dependent Patients: Results of a Pilot Cluster Randomized Controlled Trial Feasibility Study. *Substance Use & Misuse*. 2016;51(9):1104-1115. doi:10.3109/10826084.2016.1160118
886. Nyamathi AM, Nandy K, Greengold B, et al. Effectiveness of Intervention on Improvement of Drug Use Among Methadone Maintained Adults. *J Addict Dis*. 2011;30(1):6-16. Pii 931973763. doi:10.1080/10550887.2010.531669
887. Darker CD, Sweeney BP, El Hassan HO, Smyth BP, Ivers JHH, Barry JM. Brief interventions are effective in reducing alcohol consumption in opiate-dependent methadone-maintained patients: Results from an implementation study. *Drug and Alcohol Review*. 2012;31(3):348-356. doi:10.1111/j.1465-3362.2011.00349.x
888. Varshney M, Ambekar A, Lal R, Yadav D, Rao R, Mishra A. Brief Interventions for Harmful Alcohol Use in Opioid-dependent Patients on Maintenance Treatment With Buprenorphine: A Prospective Study From India. *Addictive Disorders & Their Treatment*. 2016;15(3):129-135. doi:10.1097/adt.0000000000000076
889. Rosa N, Abreu A, Mendes M. Effect of brief interventions in reducing hazardous alcohol consumption in users receiving methadone treatment. *Revista de Enfermagem Referencia*. 2015;4(6):27-34.
890. Nyamathi A, Shoptaw S, Cohen A, et al. Effect of motivational interviewing on reduction of alcohol use. *Drug Alcohol Depend*. 2010;107(1):23-30. doi:10.1016/j.drugalcdep.2009.08.021
891. Bennett GA, Edwards S, Bailey J. Helping methadone patients who drink excessively to drink less: short-term outcomes of a pilot motivational intervention. *Journal of Substance Use*. 2002;7(4):191-197. doi:10.1080/14659890215694
892. Klimas J, Fairgrieve C, Tobin H, et al. Psychosocial interventions to reduce alcohol consumption in concurrent problem alcohol and illicit drug users. *Cochrane Database Syst Rev*. 2018;12:CD009269. doi:10.1002/14651858.CD009269.pub4
893. Mattick RP, Breen C, Kimber J, Davoli M. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *Cochrane Database Syst Rev*. 2014;(2):Cd002207. doi:10.1002/14651858.CD002207.pub4
894. Nava F, Manzato E, Leonardi C, Lucchini A. Opioid maintenance therapy suppresses alcohol intake in heroin addicts with alcohol dependence: preliminary results of an open randomized study. *Prog Neuropsychopharmacol Biol Psychiatry*. 2008;32(8):1867-72. doi:10.1016/j.pnpbp.2008.08.019
895. Jones CM, Paulozzi LJ, Mack KA. Alcohol involvement in opioid pain reliever and benzodiazepine drug abuse-related emergency department visits and drug-related deaths - United States, 2010. *MMWR Morb Mortal Wkly Rep*. 2014;63(40):881-5.
896. Day C. Benzodiazepines in Combination with Opioid Pain Relievers or Alcohol: Greater Risk of More Serious ED Visit Outcomes. *The CBHSQ Report*. Substance Abuse and Mental Health Services Administration; 2013:1-9.
897. Koski A, Ojanpera I, Vuori E. Interaction of alcohol and drugs in fatal poisonings. *Hum Exp Toxicol*. 2003;22(5):281-7. doi:10.1191/0960327103ht324oa



898. McHugh RK, Geyer R, Karakula S, Griffin ML, Weiss RD. Nonmedical benzodiazepine use in adults with alcohol use disorder: The role of anxiety sensitivity and polysubstance use. *Am J Addict.* 2018;27(6):485-490. doi:10.1111/ajad.12765
899. Morel A, Grall-Bronnec M, Bulteau S, et al. Benzodiazepine dependence in subjects with alcohol use disorders: what prevalence? *Expert Opin Drug Saf.* 2016;15(10):1313-9. doi:10.1080/14740338.2016.1221922
900. Kan CC, Breteler MH, van der Ven AH, Timmermans MA, Zitman FG. Assessment of benzodiazepine dependence in alcohol and drug dependent outpatients: a research report. *Subst Use Misuse.* 2001;36(8):1085-109.
901. Substance Abuse and Mental Health Services Administration (SAMHSA), Center for Behavioral Health Statistics and Quality. *Treatment Episode Data Set (TEDS): 2004-2014. National Admissions to Substance Abuse Treatment Services. BHSIS Series S-84, HHS Publication No. (SMA) 16-4986.* SAMHSA; 2016. Accessed April 8, 2020. [https://www.samhsa.gov/data/sites/default/files/2014\\_Treatment\\_Episode\\_Data\\_Set\\_National\\_Admissions\\_9\\_19\\_16.pdf](https://www.samhsa.gov/data/sites/default/files/2014_Treatment_Episode_Data_Set_National_Admissions_9_19_16.pdf)
902. Parr JM, Kavanagh DJ, Cahill L, Mitchell G, Young RM. Effectiveness of current treatment approaches for benzodiazepine discontinuation: a meta-analysis. *Addiction.* 2009;104(1):13-24. doi:10.1111/j.1360-0443.2008.02364.x
903. Soyka M. Treatment of Benzodiazepine Dependence. *N Engl J Med.* 2017;376(12):1147-1157. doi:10.1056/NEJMra1611832
904. Pottie K, Thompson W, Davies S, et al. Deprescribing benzodiazepine receptor agonists Evidence-based clinical practice guideline. *Can Fam Physician.* 2018;64(5):339-351.
905. Breakey WR, Fischer PJ, Kramer M, et al. Health and Mental Health Problems of Homeless Men and Women in Baltimore. *JAMA.* 1989;262(10):1352-1357. doi:10.1001/jama.1989.03430100086034
906. Hwang SW. Mortality Among Men Using Homeless Shelters in Toronto, Ontario. *JAMA.* 2000;283(16):2152-2157. doi:10.1001/jama.283.16.2152
907. Fazel S, Khosla V, Doll H, Geddes J. The prevalence of mental disorders among the homeless in western countries: systematic review and meta-regression analysis. *PLoS Med.* 2008;5(12):e225. doi:10.1371/journal.pmed.0050225
908. Carter J, Zevin B, Lum PJ. Low barrier buprenorphine treatment for persons experiencing homelessness and injecting heroin in San Francisco. *Addict Sci Clin Pract.* 2019;14(1):20. doi:10.1186/s13722-019-0149-1
909. Doran KM, Rahai N, McCormack RP, et al. Substance use and homelessness among emergency department patients. *Drug Alcohol Depend.* 2018;188:328-333. doi:10.1016/j.drugalcdep.2018.04.021
910. Neisler J, Shree S, Reitzel LR, et al. Characterizing Alcohol Use Behaviors among Homeless Men and Women. *Am J Health Behav.* 2019;43(1):37-49. doi:10.5993/AJHB.43.1.4
911. Dionisi T, Mosoni C, Di Sario G, et al. Make Mission Impossible Feasible: The Experience of a Multidisciplinary Team Providing Treatment for Alcohol Use Disorder to Homeless Individuals. *Alcohol Alcohol.* 2020;55(5):547-553. doi:10.1093/alcalc/agua052

912. Stafford A, Wood L. Tackling Health Disparities for People Who Are Homeless? Start with Social Determinants. *Int J Environ Res Public Health*. 2017;14(12)doi:10.3390/ijerph14121535
913. McVicar D, Moschion J, van Ours JC. From substance use to homelessness or vice versa? *Soc Sci Med*. 2015;136-137:89-98. doi:10.1016/j.socscimed.2015.05.005
914. Dietz TL. Predictors of reported current and lifetime substance abuse problems among a national sample of U.S. homeless. *Subst Use Misuse*. 2007;42(11):1745-66. doi:10.1080/10826080701212360
915. Pauly B, Brown M, Evans J, et al. "There is a Place": impacts of managed alcohol programs for people experiencing severe alcohol dependence and homelessness. *Harm Reduct J*. 2019;16(1):70. doi:<https://dx.doi.org/10.1186/s12954-019-0332-4>
916. Pauly BB, Vallance K, Wettlaufer A, et al. Community managed alcohol programs in Canada: Overview of key dimensions and implementation. *Drug & Alcohol Review*. 2018;37 Suppl 1:S132-S139. doi:<https://dx.doi.org/10.1111/dar.12681>
917. McCormack RP, Hoffman LF, Norman M, Goldfrank LR, Norman EM. Voices of homeless alcoholics who frequent Bellevue Hospital: a qualitative study. *Ann Emerg Med*. 2015;65(2):178-186.e176. doi:<https://dx.doi.org/10.1016/j.annemergmed.2014.05.025>
918. Erickson RA, Stockwell T, Pauly BB, et al. How do people with homelessness and alcohol dependence cope when alcohol is unaffordable? A comparison of residents of Canadian managed alcohol programs and locally recruited controls. *Drug & Alcohol Review*. 2018;37 Suppl 1:S174-S183. doi:<https://dx.doi.org/10.1111/dar.12649>
919. Pauly B, King V, Smith A, et al. Breaking the cycle of survival drinking: insights from a non-residential, peer-initiated and peer-run managed alcohol program. *Drugs: Education, Prevention and Policy*. 2021;28(2):172-180. doi:10.1080/09687637.2020.1764500
920. Ongaro K. Non-beverage Alcohol Consumption and Harm Reduction Trends. Thunder Bay Drug Strategy. June 15, 2017. Available at: <https://www.thunderbay.ca/en/city-hall/resources/Documents/ThunderBayDrugStrategy/Non-Beverage-Alcohol-and-Harm-Reduction.pdf>.
921. Westenberg JN, Kamel MM, Addorisio S, et al. Non-beverage alcohol consumption among individuals experiencing chronic homelessness in Edmonton, Canada: a cross-sectional study. *Harm Reduct J*. 2021;18(1):108. doi:10.1186/s12954-021-00555-8
922. Rehm J, Kanteres F, Lachenmeier DW. Unrecorded consumption, quality of alcohol and health consequences. *Drug Alcohol Rev*. 2010;29(4):426-36. doi:10.1111/j.1465-3362.2009.00140.x
923. Hwang SW, Chambers C, Chiu S, et al. A comprehensive assessment of health care utilization among homeless adults under a system of universal health insurance. *Am J Public Health*. 2013;103 Suppl 2:S294-301. doi:10.2105/AJPH.2013.301369
924. Pauly BB, Gray E, Perkin K, et al. Finding safety: a pilot study of managed alcohol program participants' perceptions of housing and quality of life. *Harm Reduct J*. 2016;13(1):15. doi:<https://dx.doi.org/10.1186/s12954-016-0102-5>

925. Collins SE, Clifasefi SL, Nelson LA, et al. Randomized controlled trial of harm reduction treatment for alcohol (HaRT-A) for people experiencing homelessness and alcohol use disorder. *Int J Drug Policy*. 2019;67:24-33. doi:10.1016/j.drugpo.2019.01.002
926. Fentress TSP, Wald S, Brah A, et al. Dual study describing patient-driven harm reduction goal-setting among people experiencing homelessness and alcohol use disorder. *Exp Clin Psychopharmacol*. 2021;29(3):261-271. doi:10.1037/pha0000470
927. Statistics Canada. Population growth in Canada's rural areas, 2016 to 2021. <https://www12.statcan.gc.ca/census-recensement/2021/as-sa/98-200-x/2021002/98-200-x2021002-eng.pdf>
928. Statistics Canada. Heavy drinking, 2018. Accessed Aug 11, 2022. <https://www150.statcan.gc.ca/n1/pub/82-625-x/2019001/article/00007-eng.htm>
929. Lister JJ, Weaver A, Ellis JD, Himle JA, Ledgerwood DM. A systematic review of rural-specific barriers to medication treatment for opioid use disorder in the United States. *Am J Drug Alcohol Abuse*. 2020;46(3):273-288. doi:10.1080/00952990.2019.1694536
930. Chan YF, Lu SE, Howe B, Tieben H, Hoeft T, Unutzer J. Screening and Follow-Up Monitoring for Substance Use in Primary Care: An Exploration of Rural-Urban Variations. *J Gen Intern Med*. 2016;31(2):215-222. doi:10.1007/s11606-015-3488-y
931. Wang PS, Lane M, Olfson M, Pincus HA, Wells KB, Kessler RC. Twelve-Month Use of Mental Health Services in the United States: Results From the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005;62(6):629-640.
932. Edmonds AT, Bensley KM, Hawkins EJ, Williams EC. Geographic differences in receipt of addictions treatment in a national sample of patients with alcohol use disorders from the U.S. Veterans Health Administration. *Subst Abus*. 2021;42(4):559-568. doi:10.1080/08897077.2020.1803176
933. Tuckson RV, Edmunds M, Hodgkins ML. Telehealth. *N Engl J Med*. 2017;377(16):1585-1592. doi:10.1056/NEJMSr1503323
934. McKay JR, Gustafson DH, Ivey M, et al. Efficacy and comparative effectiveness of telephone and smartphone remote continuing care interventions for alcohol use disorder: a randomized controlled trial. *Addiction*. 2022;117(5):1326-1337. doi:10.1111/add.15771
935. Mark TL, Treiman K, Padwa H, Henretty K, Tzeng J, Gilbert M. Addiction Treatment and Telehealth: Review of Efficacy and Provider Insights During the COVID-19 Pandemic. *Psychiatr Serv*. 2022;73(5):484-491. doi:10.1176/appi.ps.202100088
936. Cortelyou-Ward K, Atkins DN, Noblin A, Rotarius T, White P, Carey C. Navigating the Digital Divide: Barriers to Telehealth in Rural Areas. *J Health Care Poor Underserved*. 2020;31(4):1546-1556. doi:10.1353/hpu.2020.0116
937. Brooks HL, Kassam S, Salvalaggio G, Hyshka E. Implementing managed alcohol programs in hospital settings: A review of academic and grey literature. *Drug Alcohol Rev*. 2018;37(S1):S145-S155. doi:10.1111/dar.12659

938. Vallance K, Stockwell T, Pauly B, et al. Do managed alcohol programs change patterns of alcohol consumption and reduce related harm? A pilot study. *Harm Reduct J*. 2016;13(1):13. doi:<https://dx.doi.org/10.1186/s12954-016-0103-4>
939. Podymow T, Turnbull J, Coyle D, Yetisir E, Wells G. Shelter-based managed alcohol administration to chronically homeless people addicted to alcohol. *CMAJ*. 2006;174(1):45–9.
940. Ezard, N., Dolan, K., Baldry, E., Burns, L., Day, C., Hodge, S., Cubitt, T., Loesch, B., & Mackay, T. Feasibility of a Managed Alcohol Program (MAP) for Sydney’s homeless. Canberra: Foundation for Alcohol Research and Education. 2015. Available at: <https://fare.org.au/wp-content/uploads/Feasibility-of-a-Managed-Alcohol-Program-for-Sydneys-homeless.pdf>.
941. Evans J, Semogas D, Smalley JG, Lohfeld L. “This place has given me a reason to care”: Understanding ‘managed alcohol programs’ as enabling places in Canada. *Health Place*. 2015;33:118-124. doi:10.1010/j.healthplace.2015.02.011
942. Podymow T, Turnbull J, Coyle D, Yetisir E, Wells G. Shelter-based managed alcohol administration to chronically homeless people addicted to alcohol. *CMAJ*. 2006;174(1):45-9. doi:10.1503/cmaj.1041350
943. Pauly B, Gray E, Perkin K, et al. Finding safety: a pilot study of managed alcohol program participants’ perceptions of housing and quality of life. *Harm Reduct J*. 2016;1315. doi:10.1186/s12954-016-0102-5
944. Stockwell T, Pauly BB, Chow C, et al. Does managing the consumption of people with severe alcohol dependence reduce harm? A comparison of participants in six Canadian managed alcohol programs with locally recruited controls. *Drug Alcohol Rev*. 2018;37(Suppl 1):S159-S166. doi:10.1111/dar.12618
945. Stockwell T, Zhao J, Pauly B, et al. Trajectories of Alcohol Use and Related Harms for Managed Alcohol Program Participants over 12 Months Compared with Local Controls: A Quasi-Experimental Study. *Alcohol & Alcoholism*. 2021;09:09. doi:<https://dx.doi.org/10.1093/alcalc/aga134>
946. Palpacuer C, Duprez R, Huneau A, et al. Pharmacologically controlled drinking in the treatment of alcohol dependence or alcohol use disorders: a systematic review with direct and network meta-analyses on nalmefene, naltrexone, acamprosate, baclofen and topiramate. *Addiction*. 2018;113(2):220-237. doi:10.1111/add.13974
947. Falk DE, O’Malley SS, Witkiewitz K, et al. Evaluation of drinking risk levels as outcomes in alcohol pharmacotherapy trials: a Secondary analysis of 3 randomized clinical trials. *JAMA Psychiatry*. 2019;76(4):374-381.
948. Schunemann HJ, Al-Ansary LA, Forland F, et al. Guidelines International Network: Principles for Disclosure of Interests and Management of Conflicts in Guidelines. *Ann Intern Med*. 2015;163(7):548-53. doi:10.7326/M14-1885
949. Brouwers MC, Kho ME, Browman GP, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. *CMAJ*. 2010;182(18):E839-42. doi:10.1503/cmaj.090449
950. The ADAPTE Collaboration. The ADAPTE Process: Resource Toolkit for Guideline Adaptation. Version 2.0. <https://g-i-n.net/wp-content/uploads/2021/03/ADAPTE-Resource-toolkit-March-2010.pdf>
951. British Columbia Centre on Substance Use, BC Ministry of Health, BC Ministry of Mental Health and Addictions. Provincial Guideline for the Clinical Management of High-Risk Drinking and Alcohol Use Disorder. 2019. <https://www.bccsu.ca/wp-content/uploads/2021/01/AUD-Guideline.pdf>

952. Guyatt GH, Oxman AD, Kunz R, et al. Going from evidence to recommendations. *BMJ*. 2008;336(7652):1049-51. doi:10.1136/bmj.39493.646875.AE
953. Babor TF, Higgins-Biddle JC, Saunders, JB, Monteiro MG. AUDIT: The alcohol use disorders identification test: Guidelines for use in primary health care. 2nd Ed. World Health Organization. 2001. Accessed November 7, 2021. <https://www.who.int/publications/i/item/WHO-MSD-MSB-01.6a>
954. Bradley KA, DeBenedetti AF, Volk RJ, Williams EC, Frank D, Kivlahan DR. AUDIT-C as a brief screen for alcohol misuse in primary care. *Alcohol Clin Exp Res*. 2007;31(7):1208-17. doi:10.1111/j.1530-0277.2007.00403.x
955. Crawford EF, Fulton JJ, Swinkels CM, Beckham JC, Calhoun PS. Diagnostic efficiency of the AUDIT-C in U.S. veterans with military service since September 11, 2001. *Drug Alcohol Depend*. 2013;132(1-2):101-6. doi:10.1016/j.drugalcdep.2013.01.012
956. Nordqvist C, Johansson K, Bendtsen P. Routine screening for risky alcohol consumption at an emergency department using the AUDIT-C questionnaire. *Drug Alcohol Depend*. 2004;74(1):71-5. doi:10.1016/j.drugalcdep.2003.11.010
957. Rodriguez-Martos A, Santamarina E. Does the short form of the Alcohol Use Disorders Identification Test (AUDIT-C) work at a trauma emergency department? *Subst Use Misuse*. 2007;42(6):923-32. doi:10.1080/10826080701351507
958. Vitesnikova J, Dinh M, Leonard E, Boufous S, Conigrave K. Use of AUDIT-C as a tool to identify hazardous alcohol consumption in admitted trauma patients. *Injury*. 2014;45(9):1440-4. doi:10.1016/j.injury.2014.01.004
959. Wade D, Varker T, Forbes D, O'Donnell M. The Alcohol Use Disorders Identification Test-Consumption (AUDIT-C) in the assessment of alcohol use disorders among acute injury patients. *Alcohol Clin Exp Res*. 2014;38(1):294-9. doi:10.1111/acer.12247
960. Dawson DA, Grant BF, Stinson FS, Zhou Y. Effectiveness of the derived Alcohol Use Disorders Identification Test (AUDIT-C) in screening for alcohol use disorders and risk drinking in the US general population. *Alcohol Clin Exp Res*. 2005;29(5):844-54.
961. Dawson DA, Grant BF, Stinson FS. The AUDIT-C: screening for alcohol use disorders and risk drinking in the presence of other psychiatric disorders. *Compr Psychiatry*. 2005;46(6):405-16. doi:10.1016/j.comppsy.2005.01.006
962. Frank D, DeBenedetti AF, Volk RJ, Williams EC, Kivlahan DR, Bradley KA. Effectiveness of the AUDIT-C as a screening test for alcohol misuse in three race/ethnic groups. *J Gen Intern Med*. 2008;23(6):781-7. doi:10.1007/s11606-008-0594-0
963. Gomez A, Conde A, Santana JM, Jorin A, Serrano IM, Medina R. The diagnostic usefulness of AUDIT and AUDIT-C for detecting hazardous drinkers in the elderly. *Aging Ment Health*. 2006;10(5):558-61. doi:10.1080/13607860600637729
964. Bradley KA, Bush KR, Epler AJ, et al. Two brief alcohol-screening tests From the Alcohol Use Disorders Identification Test (AUDIT): validation in a female Veterans Affairs patient population. *Arch Intern Med*. 2003;163(7):821-9. doi:10.1001/archinte.163.7.821

965. Lange S, Shield K, Monteiro M, Rehm J. Facilitating Screening and Brief Interventions in Primary Care: A Systematic Review and Meta-Analysis of the AUDIT as an Indicator of Alcohol Use Disorders. *Alcoholism: Clinical & Experimental Research*. 2019;43(10):2028-2037. doi:<https://dx.doi.org/10.1111/acer.14171>
966. Higgins-Biddle JC, Babor TF. A review of the Alcohol Use Disorders Identification Test (AUDIT), AUDIT-C, and USAUDIT for screening in the United States: Past issues and future directions. *Am J Drug Alcohol Abuse*. 2018;44(6):578-586. doi:10.1080/00952990.2018.1456545
967. Babor TF, Higgins-Biddle JC, Saunders J, Monteiro M. *The Alcohol Use Disorders Identification Test: Guidelines for Use in Primary Care. Second Edition*. World Health Organization (WHO) Department of Mental Health and Substance Dependence; 2001. Accessed April 7, 2020. [https://apps.who.int/iris/bitstream/handle/10665/67205/WHO\\_MSD\\_MSB\\_01.6a.pdf](https://apps.who.int/iris/bitstream/handle/10665/67205/WHO_MSD_MSB_01.6a.pdf)
968. Ewing JA. Detecting alcoholism. The CAGE questionnaire. *JAMA*. 1984;252(14):1905-7.
969. Cherpitel CJ. Differences in performance of screening instruments for problem drinking among blacks, whites and Hispanics in an emergency room population. *J Stud Alcohol*. 1998;59(4):420-6.
970. Cherpitel CJ. Screening for alcohol problems in the U.S. general population: a comparison of the CAGE and TWEAK by gender, ethnicity, and services utilization. *J Stud Alcohol*. 1999;60(5):705-11.
971. Bradley KA, Boyd-Wickizer J, Powell SH, Burman ML. Alcohol screening questionnaires in women: a critical review. *JAMA*. 1998;280(2):166-71.
972. O'Hare T, Tran TV. Predicting problem drinking in college students: gender differences and the CAGE questionnaire. *Addict Behav*. 1997;22(1):13-21.
973. Buchsbaum DG, Buchanan RG, Poses RM, Schnoll SH, Lawton MJ. Physician detection of drinking problems in patients attending a general medicine practice. *J Gen Intern Med*. 1992;7(5):517-21.
974. Conigliaro J, Kraemer K, McNeil M. Screening and identification of older adults with alcohol problems in primary care. *J Geriatr Psych Neur*. 2000;13(3):106-14. doi:10.1177/089198870001300303
975. Deady M, Network of Alcohol and Other Drug Agencies (NADA). *A review of screening, assessment and outcome measures for drug and alcohol settings*. NSW Health Department; 2009. Accessed April 7, 2020. [http://www.drugsandalcohol.ie/18266/1/NADA\\_A\\_Review\\_of\\_Screening%2C\\_Assessment\\_and\\_Outcome\\_Measures\\_for\\_Drug\\_and\\_Alcohol\\_Settings.pdf](http://www.drugsandalcohol.ie/18266/1/NADA_A_Review_of_Screening%2C_Assessment_and_Outcome_Measures_for_Drug_and_Alcohol_Settings.pdf).
976. Knight JR, Shrier LA, Bravender TD, Farrell M, Vander Bilt J, Shaffer HJ. A new brief screen for adolescent substance abuse. *Arch Pediat Adol Med*. 1999;153(6):591-6.
977. Levy SJL, Williams JF, Ryan SA, et al. Substance Use Screening, Brief Intervention, and Referral to Treatment. *Pediatrics*. 2016;138(1)e20161210. doi:10.1542/peds.2016-1210
978. Patton KA, Connor JP, Sheffield J, Wood A, Gullo MJ. Additive effectiveness of mindfulness meditation to a school-based brief cognitive-behavioral alcohol intervention for adolescents. *J Consult Clin Psychol*. 2019;87(5):407-421. doi:10.1037/ccp0000382 10.1037/ccp0000382.supp (Supplemental)

979. Dhalla S, Zumbo BD, Poole G. A review of the psychometric properties of the CRAFFT instrument: 1999-2010. *Curr Drug Abuse Rev.* 2011;4(1):57-64.
980. D'Amico EJ, Parast L, Meredith LS, Ewing BA, Shadel WG, Stein BD. Screening in Primary Care: What Is the Best Way to Identify At-Risk Youth for Substance Use? *Pediatrics.* 2016;138(6)e20161717. doi:10.1542/peds.2016-1717
981. Burd L, Klug MG, Martsof JT, Martsof C, Deal E, Kerbeshian J. A staged screening strategy for prenatal alcohol exposure and maternal risk stratification. *J R Soc Promot Health.* 2006;126(2):86-94.
982. Russell M, Martier SS, Sokol RJ, et al. Screening for pregnancy risk-drinking. *Alcohol Clin Exp Res.* 1994;18(5):1156-61.
983. Sokol RJ, Martier SS, Ager JW. The T-ACE questions: practical prenatal detection of risk-drinking. *Am J Obstet Gynecol.* 1989;160(4):863-8; discussion 868-70.
984. Yonkers KA, Gotman N, Kershaw T, Forray A, Howell HB, Rounsaville BJ. Screening for Prenatal Substance Use Development of the Substance Use Risk Profile-Pregnancy Scale. *Obstet Gynecol.* 2010;116(4):827-833. doi:10.1097/AOG.0b013e3181ed8290
985. National Institute on Alcohol Abuse and Alcoholism (NIAAA). *Alcohol Use Disorder: A Comparison Between DSM-IV and DSM-5. NIH Publication No. 13-7999.* 2016. Accessed April 7, 2020. <https://pubs.niaaa.nih.gov/publications/dsmfactsheet/dsmfact.pdf>
986. The Canadian Medical Protective Association. *Medical-legal handbook for physicians in Canada.* 2016. Accessed May 31, 2019. [www.cmpa-acpm.ca](http://www.cmpa-acpm.ca)
987. Skinner W, Canadian Centre on Substance Use and Addiction (CCSA). *The Essentials of Motivational Interviewing.* CCSA; 2017. Accessed April 7, 2020. <http://www.ccsa.ca/Resource%20Library/CCSA-Motivational-Interviewing-Summary-2017-en.pdf>
988. Substance Abuse and Mental Health Services Administration (SAMHSA), Center for Substance Abuse Treatment. *Enhancing Motivation for Change in Substance Abuse Treatment. Treatment Improvement Protocol (TIP) Series, No. 35. HHS Publication No. (SMA) 13-4212.* 2013. Accessed May 23, 2023. <https://store.samhsa.gov/product/TIP-35-Enhancing-Motivation-for-Change-in-Substance-Use-Disorder-Treatment/PEP19-02-01-003>
989. Centers for Disease Control and Prevention. *Planning and Implementing Screening and Brief Intervention for Risky Alcohol Use: A Step-by-Step Guide for Primary Care Practices.* Centers for Disease Control and Prevention, National Center on Birth Defects and Developmental Disabilities; 2014. Accessed April 7, 2020. <https://www.cdc.gov/ncbddd/fasd/documents/alcoholsbiimplementationguide.pdf>
990. Gonzalez S, Grubb J, Kowalchuck A, et al. *Addressing Alcohol Use Practice Manual: An Alcohol Screening and Brief Intervention Program.* Accessed April 7, 2020. [https://www.aafp.org/dam/AAFP/documents/patient\\_care/alcohol/alcohol-manual.pdf](https://www.aafp.org/dam/AAFP/documents/patient_care/alcohol/alcohol-manual.pdf)
991. National Institute on Alcohol Abuse and Alcoholism (NIAAA). *Helping Patients Who Drink Too Much: A Clinician's Guide. NIH Publication No. 05-3769.* . 2005. Accessed May 23, 2023. <https://pubs.niaaa.nih.gov/publications/clinicianGuide/guide/intro/data/resources/Clinicians%20Guide.pdf>

992. Eloma AS, Tucciarone JM, Hayes EM, Bronson BD. Evaluation of the appropriate use of a CIWA-Ar alcohol withdrawal protocol in the general hospital setting. *Am J Drug Alcohol Abuse*. 2018;44(4):418-425. doi:<http://dx.doi.org/10.1080/00952990.2017.1362418>
993. Waye C, Wong M, Lee S. Implementation of a CIWA-Ar alcohol withdrawal protocol in a veterans hospital. *South Med J*. 2015;108(1):23-28. doi:<https://dx.doi.org/10.14423/SMJ.0000000000000216>
994. Jones AW. Evidence-based survey of the elimination rates of ethanol from blood with applications in forensic casework. *Forensic Sci Int*. 2010;200(1-3):1-20. doi:10.1016/j.forsciint.2010.02.021
995. Cowan JM, Burris JM, Hughes JR, Cunningham MP. The Relationship of Normal Body Temperature, End-Expired Breath Temperature, and BAC/BrAC Ratio in 98 Physically Fit Human Test Subjects. *J Anal Toxicol*. 2010;34(5):238-242. doi:10.1093/jat/34.5.238
996. Jones AW, Andersson L. Comparison of ethanol concentrations in venous blood and end-expired breath during a controlled drinking study. *Forensic Sci Int*. 2003;132(1):18-25. Pii s0379-0738(02)00417-6. doi:10.1016/s0379-0738(02)00417-6
997. McMicken D, Liss JL. Alcohol-Related Seizures. Review. *Emerg Med Clin North Am*. 2011;29(1):117-124. doi:<http://dx.doi.org/10.1016/j.emc.2010.08.010>
998. Vaaramo K, Puljula J, Tetri S, Juvela S, Hillbom M. Predictors of new-onset seizures: a 10-year follow-up of head trauma subjects with and without traumatic brain injury. *Journal of Neurology, Neurosurgery & Psychiatry*. 2014;85(6):598-602. doi:<https://dx.doi.org/10.1136/jnnp-2012-304457>
999. Clorazepate (clorazepate dipotassium capsules) Product Monograph. Submission Control No: 156856. AA Pharma Inc., Vaughan, Ontario, Canada. Available at: [https://pdf.hres.ca/dpd\\_pm/00017097.PDF](https://pdf.hres.ca/dpd_pm/00017097.PDF).
1000. VALIUM (diazepam) Product Monograph; 5 mg tablets. Submission Control No: 212691. Hoffman LaRoche Ltd., Mississauga, Canada. Available at: [https://pdf.hres.ca/dpd\\_pm/00044869.PDF](https://pdf.hres.ca/dpd_pm/00044869.PDF).
1001. <sup>TC</sup>Oxepam tablets (Oxazepam, USP) Product Monograph. Submission Control No: 177866. Biomed 2002 Inc., Ville Mont-Royal, Quebec, Canada. Available at: [https://pdf.hres.ca/dpd\\_pm/00027688.PDF](https://pdf.hres.ca/dpd_pm/00027688.PDF).
1002. <sup>Pr</sup>pms-VALPROIC ACID Product Monograph; capsules, USP 250 mg; enteric-coated capsules 500 mg; valproic acid oral solution, USP 250 mg/5 mL. Submission Control No. 203416. Pharmascience Inc., Montreal, Canada. Available at: [https://pdf.hres.ca/dpd\\_pm/00038561.PDF](https://pdf.hres.ca/dpd_pm/00038561.PDF).
1003. <sup>Pr</sup>Catapres® (clonidine hydrochloride) Product Monograph. Submission Control No: 154435. Boehringer Ingelheim (Canada) Ltd., Burlington, Ontario. Available at: [https://pdf.hres.ca/dpd\\_pm/00016975.PDF](https://pdf.hres.ca/dpd_pm/00016975.PDF).
1004. Bjorkqvist SE, Isohanni M, Makela R, Malinen L. Ambulant treatment of alcohol withdrawal symptoms with carbamazepine: a formal multicentre double-blind comparison with placebo. *Acta Psychiatr Scand*. 1976;53(5):333-42.
1005. Hillbom M, Tokola R, Kuusela V, et al. Prevention of alcohol withdrawal seizures with carbamazepine and valproic acid. *Alcohol*. 1989;6(3):223-6.



1006. Reoux JP, Saxon AJ, Malte CA, Baer JS, Sloan KL. Divalproex sodium in alcohol withdrawal: a randomized double-blind placebo-controlled clinical trial. *Alcohol Clin Exp Res*. 2001;25(9):1324-9.
1007. Rosenthal RN, Perkel C, Singh P, Anand O, Miner CR. A pilot open randomized trial of valproate and phenobarbital in the treatment of acute alcohol withdrawal. *Am J Addict*. 1998;7(3):189-97. doi:10.3109/10550499808998350
1008. Yoon G, Kim SW, Petrakis IS, Westermeyer J. High-dose naltrexone treatment and gender in alcohol dependence. *Clin Neuropharmacol*. 2016;39(4):165-168.
1009. Cornish JW, Metzger D, Woody GE, et al. Naltrexone pharmacotherapy for opioid dependent federal probationers. *J Subst Abuse Treat*. 1997;14(6):529-534.
1010. Jefee-Bahloul H, Jorandby L, AJ A. Topiramate treatment of alcohol use disorder in clinical practice. *J Addict Med* 2016;13(1):23-27.
1011. Carvalho AF, Heilig M, Perez A, Probst C, Rehm J. Alcohol use disorders. *Lancet*. 2019;394(10200):781-792.
1012. Mason BJ, Quello S, Goodell V, Shadan F, Kyle M, Begovic A. Gabapentin Treatment for Alcohol Dependence A Randomized Clinical Trial. *JAMA Internal Medicine*. 2014;174(1):70-77. doi:10.1001/jamainternmed.2013.11950



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