Alcohol use disorders are common in developed countries, where alcohol is cheap, readily available, and heavily promoted. Common, mild disorders often remit in young adulthood, but more severe disorders can become chronic and need long-term medical and psychological management. Doctors are uniquely placed to opportunistically assess and manage alcohol use disorders, but in practice diagnosis and treatment are often delayed. Brief behavioural intervention is effective in primary care for hazardous drinkers and individuals with mild disorders. Brief interventions could also encourage early entry to treatment for people with more-severe illness who are underdiagnosed and undertreated. Sustained abstinence is the optimum outcome for severe disorder. The stigma that discourages treatment seeking needs to be reduced, and pragmatic approaches adopted for patients who initially reject abstinence as a goal. To engage people in one or more psychological and pharmacological treatments of equivalent effectiveness is more important than to advocate a specific treatment. A key research priority is to improve the diagnosis and treatment of most affected people who have comorbid mental and other drug use disorders.

Introduction

Alcohol use disorders are among the most common and undertreated mental disorders in developed countries. Affected individuals have impaired control over their alcohol consumption and continue to drink despite the serious adverse effects on their health and the lives of their spouses, children, family members, friends, and workmates.

Applying Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) diagnostic criteria, in 2012–13 36·0% of male and 22·7% of female adults in the USA met the criteria for alcohol use disorders at some time in their lives, and 17·6% of men and 10·4% of women did so in the past year. Differences between the sexes have narrowed because women’s drinking patterns have become similar to men’s in recent birth cohorts. The risk of development of an alcohol use disorder increases with the frequency of binge drinking, although most heavy drinkers do not meet the criteria for alcohol dependence.

The disorders are most prevalent in young adulthood (age 18–29 years). Mild disorders often remit as young adults enter the labour market, marry, and assume responsibility for children. More-severe alcohol use disorders are one of the most undertreated mental disorders, with less than 15% of patients receiving treatment. The first episode of treatment is delayed until the disorder is well established, typically after age 30 years. Doctors are uniquely placed to opportunistically assess and manage alcohol use disorders. In this Seminar, we describe effective behavioural and pharmacological treatments and emerging research directions.

Alcohol-related burden of disease

Alcohol consumption is causally linked to 60 different diseases. The major causes of premature death to which it contributes are injury, alcoholic liver disease, heart disease and stroke, cancers, and gastrointestinal disease. Cardiovascular benefits might be gained from very low levels of alcohol use for middle-aged men (typically age 40–60 years), but these benefits are most likely to be seen in developed countries where risk of heart disease is high. Even in these countries, the total harm caused by alcohol use in the population far outweighs the modest cardiovascular benefits.

Alcohol use contributes to around 4% of the global burden of disease. This contribution is equivalent to that of tobacco smoking because alcohol use causes more premature deaths in young adults than
does tobacco smoking.\textsuperscript{11} This burden is greatest in developed countries, where more people regularly drink to intoxication and other causes of mortality are low.\textsuperscript{11} The harms caused by alcohol are related to the average volume of alcohol consumed and the pattern of drinking. The risk of harm rises steeply when more than 10–20 g of alcohol is consumed per day. Episodic drinking to intoxication greatly increases the risks of accidents, injuries, violence, and heart disease.\textsuperscript{11}

People with alcohol use disorders account for around half of all the alcohol-related harm in developed societies.\textsuperscript{12} The remainder arises from accidents, assaults, and suicides in young adults, especially men, who engage in episodic drinking to intoxication, but most of whom do not meet the criteria for alcohol use disorders. The harms arising from both intoxication and such disorders need to be prevented to reduce the burden of alcohol-related harm.\textsuperscript{5}

Diagnostic systems

Version 10 of the International Classification of Diseases\textsuperscript{13} distinguishes “harmful use” from “dependence”, whereas DSM-III\textsubscript{14} to DSM-IV-TR\textsubscript{15} (1980–2013) distinguished between “alcohol abuse” and “alcohol dependence”. These two categories have been combined in DSM-5\textsubscript{2} into one category—“alcohol use disorder”—because of empirical evidence that symptoms of such disorders vary in severity along one dimension (appendix).\textsuperscript{16}

According to DSM-5, at least two of 11 symptoms need to be present for diagnosis of an alcohol use disorder. Severity is assessed by the number of symptoms recognised (appendix).

Behavioural and neurobiological effects

Alcohol affects a wide range of neurotransmitter systems in the brain that are implicated in cognition, emotion, and motivation.\textsuperscript{17} At low doses, alcohol has rewarding, anxiolytic, and socially facilitating effects. As the dose increases, alcohol produces cognitive and psychomotor impairment that increases the risks of injury, and it also disrupts emotional regulation in ways that contribute to assaults.

The pleasurable effects of alcohol provide an explanation for the initiation and persistence of alcohol use and a part explanation for the development of alcohol use disorders. The repeated pairing of environmental cues and rewards enhances alcohol’s subjective and physiological effects via conditioning\textsuperscript{18} and social and cognitive learning about the effects of alcohol (ie, alcohol expectancies). Outcome expectancies (eg, tension reduction and increased confidence) and individuals’ beliefs about their ability to refrain from drinking (ie, self-efficacy) contribute to the risk of development of alcohol use disorders.\textsuperscript{19} Individuals with high alcohol expectancies and low self-efficacy are at increased risk of problem drinking.\textsuperscript{19} Both factors can be modified by cognitive behaviour therapies (table 1).\textsuperscript{28}

Alcohol crosses the blood–brain barrier and interacts with many neurotransmitter systems rather than a single molecular target. It increases GABA, glycine, nicotinic acetylcholine, and serotonin activity. It also indirectly increases dopamine, opioid, and endocannabinoid activity (figure) and inhibits glutamate transmission. These complex effects contribute to acute intoxication. The pleasurable effects seem to be mediated by increased dopaminergic transmission in the mesolimbic reward system.
The clinical features of alcohol dependence include tolerance and withdrawal. With repeated dosing, neurotransmitter responses are reduced, and increased doses of alcohol are needed to produce the same effect. Abrupt cessation produces rebound effects that are experienced as withdrawal symptoms. Each of the neurotransmitter systems affected by alcohol has been targeted with some success by pharmacological treatments. An increased understanding of the neurobiology holds promise to translate into improved targeted drug treatments for alcohol dependence.

Risk factors for alcohol use disorders

Patients and their families need to understand that alcohol use disorders are not merely a result of an individual moral failing but arise from the combined effects of many personal, social, and biological factors. The prevalence of alcohol use disorders in the population is increased in cultures that encourage adults to drink to intoxication. These cultures typically make alcohol readily available at low cost, allow use in everyday settings, and create a social milieu in which drinking to intoxication is socially approved and promoted by ubiquitous alcohol advertisements.31 Early initiation and hazardous alcohol consumption in adolescence predict a raised risk of development of alcohol use disorders in adulthood.32 Other risk factors include a family history of alcohol dependence, low parental monitoring and poor family support, childhood conduct and mood disorders, low self-control and impulsivity, and positive alcohol expectancies.33 Peer alcohol use is one of the strongest predictors of adolescent alcohol use.33 People with a family history of early-onset alcohol use disorders in several male and female first-degree relatives are at high risk of development of such disorders.34 This pattern shows the combined effects of increased genetic risk and a childhood environment in which parents model heavy drinking.

Twin studies estimated that 50–70% of the risk of alcohol use disorders is attributable to additive genetic factors.35 The strongest genetic association is with a genotype that reduces the risk. Alcohol dehydrogenase and the mitochondrial form of aldehyde dehydrogenase (ALDH2) are liver enzymes that metabolise alcohol. The ALDH2 genotype is expressed by two primary alleles known as ALDH2*1 and ALDH2*2. Carriers of ALDH2*2 (ie, those with a single copy of the allele) have impaired alcohol metabolism. If they drink alcohol, they usually have facial flushing, sweating, tachycardia, nausea, vomiting, and headache, which protect against development of alcohol use disorders.36 This polymorphism is carried by roughly 23% of all Asian populations (range 1–53%) but is rare in Europeans.36 Risk alleles have been identified that modestly increase the risk of alcohol use disorders.37 These alleles affect neurotransmitter responses to alcohol in the dopaminergic, opioidergic, GABAergic, serotonergic, cholinergic, and glutamatergic systems. These gene variations each contribute less than 1% of the genetic risk for alcohol use disorders.38 The hope is that the remaining contributors to genetic risk will be identified39 by higher-powered genome-wide association studies that examine the differences between cases and controls across large numbers of single-nucleotide polymorphisms.

Clinical presentation, signs, and symptoms in primary care

Drinkers often underestimate their alcohol consumption40 because standard drink units are usually poorly understood and vary between 8 g in the UK and 19·75 g in Japan.41 Recommended low-risk alcohol consumption values also vary between countries, but typical ranges are 20–40 g per day.
(<200 g per week) for men and 10–30 g per day (<140 g per week) for women. With the variations in glass size and average pours, these values roughly equate to two to three drinks (eg, glasses of wine, shots of whisky) per day for men and one to two drinks per day for women. These values approximate Rehm and colleagues’ estimated lifetime risk thresholds for alcohol-related mortality from chronic illness (two drinks per day) and acute injury (three to four drinks per day). Medical and other health professionals should be familiar with national safe drinking guidelines and the alcohol content of widely consumed beverages. Age of onset and duration of alcohol use, pattern of use, and circumstances of any periods of abstinence should be assessed.

Roughly half of individuals with alcohol use disorders remain undiagnosed if doctors rely only on their clinical judgment. Structured questions about alcohol use and brief questionnaires such as CAGE, the Michigan Alcohol Screening Test, and Alcohol Use Disorders Identification Test (AUDIT) can identify patients who need further assessment. The ten-item WHO AUDIT is useful in detection of problem drinking in a range of clinically and culturally diverse populations (sensitivity and specificity typically 80–90%). It takes less than 2 min to complete and is easily scored. Scores of 8 or higher suggest hazardous drinking, and scores of 16 or higher suggest probable alcohol dependence. A brief version of the AUDIT (AUDIT C), consisting of the first three questions (how often is alcohol consumed, how many alcoholic drinks are typically drunk in a day, and how often are six or more drinks consumed), has similar psychometric properties to the full scale. A cutoff score of 3 has been suggested for hazardous drinking and 4 for possible alcohol use disorder.

Management

Patients are most likely to be diagnosed and managed in a medical setting—eg, when they are treated in hospital for an alcohol-related injury, or gastrointestinal or liver disease. The adverse effects of their alcohol use might be discovered in the course of other treatment—eg, preparation for surgery or via abnormal blood tests. A patient seeking treatment for an alcohol use disorder is less common.

Clinical assessment should obtain a detailed history of alcohol use, the symptoms of alcohol use disorder (panel), and the details of the last drinking session. The use of other substances, including tobacco and prescription drugs, should be assessed. Patients should be asked about any harm to their physical and mental health, social situation, including interpersonal and forensic issues, and their work. Their insight into the contribution of alcohol to their health problem and their motivation to change their drinking habits should be assessed. Inquiries should be made about any previous treatment for alcohol use disorders, its outcome, and any mental health symptoms, diagnoses, or treatment.

Physical examination should begin by assessment of symptoms of intoxication and withdrawal. Intoxication manifests in slurred speech, ataxia, and inappropriate affect. Alcohol value should be measured in the blood or breath. The earliest signs of withdrawal are restlessness, tachycardia, and a fine action tremor.

A neurological examination should look for signs of Wernicke’s encephalopathy or acute intracranial lesion. The classic triad of confusion, ataxia, and nystagmus suggests Wernicke’s encephalopathy, but most cases will have only one or two signs. Tests should be done for upper motor neuron signs, particularly lateralisers signs, such as pupillary asymmetry, that suggest an intracranial lesion. Orientation, short-term memory, mental state, insight, and motivation should be assessed, as should...
common cerebellar signs such as nystagmus and ataxia. A general medical examination should identify other physical signs of alcohol use disorders (panel) and exclude unrelated disorders. In particular, alcohol is an under-recognised leading reversible cause of hypertension.\textsuperscript{51,52}

Diagnostic investigations

Standard blood tests, including liver tests and mean corpuscular volume of red blood cells (MCV), are often abnormal in people with alcohol use disorders, but these tests have low sensitivity and specificity.\textsuperscript{53,54} γ-glutamyl transpeptidase (gGT) is the most widely used marker but is of little value because of poor sensitivity and specificity (table 2): gGT can detect only about one in five cases of heavy drinking.\textsuperscript{55} Its predictive value is greatest in overweight (body-mass index [BMI] >25 kg/m\textsuperscript{2}) men older than 40 years.\textsuperscript{55–57} It is rarely helpful in detection of heavy drinking in young lean women (age <20 years).\textsuperscript{58} The most common cause of high gGT is an increased BMI.\textsuperscript{55} Other causes of liver disease and some drugs reduce the specificity of gGT as a marker of alcohol use disorders. Uric acid, triglycerides, MCV, and liver enzymes are commonly raised but are not specific to alcohol use disorders. The presence of several abnormalities is uncommon but suggestive of alcohol use disorders.

Biomarkers for alcohol use that are more sensitive and specific than standard clinical assays exist, but they are not widely used because of their high cost and limited availability. These biomarkers include carbohydrate-deficient transferrin, ethyl glucuronide, ethyl sulphate, phosphatidyl ethanol, and fatty acid ethyl esters (table 2).\textsuperscript{54}

Once a disorder is recognised, full blood count and biochemical, glucose, and liver tests are important in assessment of medical complications. Alcohol use disorders are associated with nutritional disorders, but vitamin testing is costly and not routinely recommended. Imaging studies (eg, in the brain and liver) should be done only when clinically indicated.

Acute management

A heavy drinker who cannot be roused should be admitted to hospital to prevent fatal aspiration. Airway protection, hydration, management of seizures, and monitoring of blood glucose and ketoacidosis might be necessary. Individuals with alcohol intoxication who show aggressive behaviour might need intramuscular sedation in the emergency department.\textsuperscript{59} Supportive care protects unconscious patients from injury. Patients should be monitored for withdrawal as intoxication resolves.

Withdrawal can be managed in the community, primary care, specialist services, or hospital, according to its severity and the availability of services. The most widely used withdrawal assessment scale is the clinical institute withdrawal assessment for alcohol (revised version; CIWA-Ar).\textsuperscript{60} It is sensitive, reproducible, and can be used with minimum training, but a high score can show intercurrent illnesses rather than alcohol withdrawal. No withdrawal scale has been validated in the inpatient setting, in which comorbidity is prevalent. Rating scores should be checked carefully before treatment is modified. Serious comorbidity is probably better managed without use of a scale.

The most widely used drugs for management of alcohol withdrawal are benzodiazepines\textsuperscript{61} These drugs can be given by fixed (eg, day 1: 20 mg four times; day 2: 10 mg four times; day 3: 10 mg twice; day 4: 5 mg twice; day 5: 5 mg up to twice if needed; day 6: cease), symptom-triggered, or
front-loading regimens. High doses are generally needed in the first 24 h. They are then tapered over the next few days and cease within 5–7 days of initial treatment. Symptom-triggered dosing needs monitoring of withdrawal severity according to the CIWA-Ar, dose adjustment when needed, and close nursing care. Fixed dosing is most practical in less well monitored settings, including home detoxification.

Inpatients with comorbidities could be most safely managed by fixed dosing with daily clinical review. Front loading via hourly dosing of 10–20 mg diazepam is appropriate for those with severe withdrawal symptoms. It is ceased once the patient settles. Risks of benzodiazepines include oversedation and benzodiazepine dependence. In jaundiced patients with liver failure, oxazepam is preferred to diazepam because it has a short half-life and no active metabolites. Sedation is hazardous in patients with head injury or respiratory failure, and should be done only with specialist oversight in high-dependency units.

Potentially fatal complications of alcohol withdrawal include seizures and delirium. Withdrawal delirium (ie, delirium tremens) occurs in roughly 5% of patients. Few controlled trials to direct management or dosing regimens have been done. Delirium is probably best managed with intravenous benzodiazepines and antipsychotic drugs in an inpatient or intensive-care unit setting. Other agents trialled to treat withdrawal include baclofen, gabapentin, carbamazepine, and valproic acid. The few studies of these drugs have had mixed findings. Until better evidence is obtained, these drugs should not be used in routine clinical practice.

Many patients do not need sedation; they do well with reassurance in a safe, alcohol-free environment. Supportive care should monitor and manage dehydration, electrolyte disorders, and infections, and monitor complications. The risk of relapse to alcohol use after withdrawal exceeds 90%, so further treatment is needed to reduce this risk.

Wernicke-Korsakoff syndrome is a devastating neurological complication of alcohol use disorders that can produce lifelong disability or death. Symptoms such as confusion, ataxia, or nystagmus often emerge during alcohol withdrawal. The evidence base to guide treatment of the syndrome is poor, and no randomised controlled trials have been done in the past decade. Guidelines are related to clinical experience, pathophysiology where known, and the ease of thiamine supplementation.

Prophylactic parenteral thiamine should be given in every case. The first parenteral dose of thiamine should be given in the emergency department without delay. Present practice is to give thiamine before any dextrose, although a recent review reported little evidence that intravenous dextrose precipitates the syndrome. For prophylaxis, a parenteral dose of 200 mg per day is recommended. For treatment of suspected or established Wernicke-Korsakoff syndrome, the recommended dose is 500 mg given intravenously three times per day for 2–3 days. Further treatment is guided by response. Oral thiamine treatment should be continued until sustained abstinence is achieved, and indefinitely if the person continues to drink.

**Differential diagnosis**

In epidemiological surveys, half of all individuals with a lifetime history of alcohol use disorders have at least one other mental health disorder. Treatment studies typically exclude patients with concurrent psychiatric diagnoses, making it difficult to advise how to manage the most common forms of comorbidity, such as anxiety and mood (so-called internalising) disorders.
comprehensive psychiatric assessment is essential to identify the primary disorder or disorders (psychiatric or alcohol use disorder) for treatment planning. Engagement of patients in treatment is crucial, and motivational strategies might assist (table 1). Mood symptoms typically reduce with abstinence, but treatment might be needed for mood and anxiety disorders that do not remit. Research into how to best manage patients with comorbid alcohol use disorders and other mental disorders, or drug and alcohol use disorders, is scarce. A research priority is to do high-quality treatment trials of patients with alcohol use disorders who have the most common forms of psychiatric comorbidity.

Most individuals also have another substance use disorder. At least half are tobacco smokers and a third have another drug use disorder. Alcohol and tobacco potentiate the risk for head and neck cancers. People using more than one substance have poorer mental health than do those using only one substance. Alcohol and benzodiazepine use is often overlooked. Patients who also use more than one substance have poor outcomes from behavioural treatment.

Heavy drinkers who are prescribed CNS depressants and opioids need to be carefully monitored. Dependence on both alcohol and opioid is dangerous. Most fatal and non-fatal opioid overdoses occur in combination with use of alcohol or benzodiazepine, or both, often as a result of respiratory depression. Whether detoxification is needed for individuals with dependence on other substances needs to be established; if so, evidence-based approaches should be used.

Alcoholic liver disease is the most common serious medical complication of alcohol use disorders. The risk of alcoholic liver disease is highest in overweight (BMI >25–30 kg/m²) and obese (BMI >30 kg/m²) individuals, in women, and in those with a family history of alcoholic liver disease, hereditary haemochromatosis, and chronic viral hepatitis B and C. Patients presenting with alcoholic liver disease usually have less severe alcohol use disorder and have consumed less alcohol than those without such disease.

Alcoholic liver disease is recognised by clinical hepatomegaly or abnormal ultrasound. The liver tests are abnormal and, in most cases, have dominant gGT concentrations and higher concentrations of aspartic acid aminotransferase than alanine aminotransferase. Treatment options are few. Abstinence is essential in all but trivial cases of alcoholic liver disease and improves survival. Few treatment trials have been done for people presenting with alcoholic liver disease, but one trial has shown baclofen to be safe and effective.

**Brief behavioural interventions**

Brief interventions are recommended for all patients who are drinking hazardenously. They usually last 5–20 min and typically include one to three sessions. They provide information and advice on safe levels of consumption and might include motivational inter-viewing (table 1). More frequent, brief interventions are usually more effective than one extended session. Brief interventions are moderately effective and can reduce problem drinking in primary-care patients and inpatients; more-intensive interventions in emergency departments and sexual health services can also do so. Studies have been predominantly done in middle-aged male drinkers. Variations in the content and intensity of brief interventions create uncertainty over how they work, and more research is needed to assess their benefits.
Screening and brief interventions could encourage people with alcohol use disorders to receive treatment early. Patients scoring 0–7 in the AUDIT in primary care should be given basic alcohol education, those scoring 8–15 given straightforward advice on reduction of hazardous drinking, those scoring 16–19 given straightforward advice in addition to brief counselling and continued monitoring, and those scoring 20–40 referred for specialist assessment.

Relapse prevention

Follow-up studies of untreated patients show average abstinence of 21% for up to 1 year. Most patients reduce their frequency of heavy drinking because of illness, adverse social effects, or the urging of family members. After formal treatment, meta-analyses find abstinence ranging from 25% to 43%, dependent on treatment intensity and length of follow-up.

Behavioural treatments improve outcomes (table 1). These approaches differ in rationale but seem to be similarly effective. In practice, different behavioural approaches are often combined. Motivational interviewing is most widely used to engage patients in treatment so that cognitive and behavioural approaches can modify dysfunctional cognitions and address skill deficits. Treatment can take place on an individual or a group basis. Engagement of spouses of people with alcohol use disorders in joint therapy is effective. 12-step facilitation is the most widely recognised group intervention.

Different pharmacotherapies for relapse prevention are similarly effective. Three drugs have been approved by the equivalent of the US Food and Drug Administration (eg, Therapeutic Goods Administration in Australia) to treat alcohol use disorders by maintenance of abstinence: naltrexone, acamprosate, and disulfiram (table 3). Naltrexone and acamprosate have similar efficacy (number needed to treat 9–12). Meta-analyses show that acamprosate is probably more effective in maintenance of abstinence whereas naltrexone is best at prevention of heavy drinking. The combination of acamprosate and naltrexone resulted in fewer relapses than did single agents in some studies but not in the largest study done so far. No robust data for optimum length of pharmacotherapy exist because the average duration of treatment trials is 6 months for acamprosate and 3 months for naltrexone.

Two recent meta-analyses found disulfiram effective only when dosing was supervised, and little evidence of longer-term effectiveness exists. Disulfiram might be suitable only for highly motivated, supervised patients who will also do well with other pharmacotherapies that have fewer adverse effects and contraindications.

Nalmefene has been approved by the European Medicines Agency to reduce alcohol use rather than achieve abstinence (table 3). It is taken when the patient feels at risk of drinking. In one large multisite outpatient trial, nalmefene significantly reduced heavy drinking days and daily consumption in patients who continued to drink. Its use has a clinical and public health justification. It helps heavy drinkers to reduce their average consumption. It is also a cost-effective way to reduce the population burden of alcohol-related disease. The available evidence does not provide clear recommendations about which drug or psychosocial intervention is best for which patients. Therefore, best practice is for physicians to encourage their patients to choose from available treatments that have proved safe and effective.

Alcoholics Anonymous is a widely used intervention for alcohol use disorders. Evidence for its effectiveness is mixed (table 1). Many patients find the social support provided by 12-step self-help...
groups useful in maintenance of abstinence, especially if they have no other social support. Those who have chosen abstinence as a goal should be encouraged to attend these meetings. The SMART recovery model is an alternative self-help approach for individuals who reject the religious aspects of the 12-step approach.

Alcohol use disorders are highly stigmatised, and many people with them do not seek treatment for this reason. Less stigmatising attitudes could be encouraged by a diagnostic approach that emphasises a continuum of symptoms rather than a dichotomous diagnostic category. If so, the adoption of a severity continuum in DSM-5 could increase treatment engagement.

A crucial aspect is to engage patients in any evidence-based treatment. The similar effectiveness of behavioural and pharmacological approaches suggests that patients should be given a choice of clinically indicated treatments. Patient-centred care and shared decision making also help to destigmatise alcohol use disorders and engage patients in treatment.

Another important aspect is to increase patients’ motivation to address their drinking habits, resolve their ambivalence about alcohol use, set realistic goals, and engage in decision making. Patients with more-severe disorders (eg, high levels of dependence, high craving, end-organ damage, and severe social disruption) should be encouraged to add drug treatment to their existing treatment. Further field testing will examine whether the DSM-5 severity index (appendix) could guide health professionals and patients in their choice of the type and intensity of treatment.

Sustained abstinence is the optimum outcome for most patients with an alcohol use disorder. Risk of relapse reduces considerably after 10–14 weeks of abstinence. Abstinence is recommended for those with more-severe alcohol use disorders, end-organ damage, and severe social disruption. The treatment goal will affect pharmacotherapy choice. Meta-analyses suggest that acamprosate and disulfiram might be better suited to abstinence-oriented treatment, whereas naltrexone and nalmefene might be better choices when reduced or controlled drinking is the goal.

Few patients with severe alcohol use disorders can return to moderate drinking, but many initially reject abstinence as a goal, which is often a barrier to their engagement in treatment. A pragmatic approach is to clinically engage with patients who insist on controlled or reduced-risk drinking as the goal of treatment. This approach enables a therapeutic relationship to develop and leaves open the future modification of treatment goal—eg, the failure to achieve control over drinking could suggest the need for abstinence.

Patients who are unresponsive to treatment in primary care and as outpatients might need structured residential treatment in a therapeutic community or rehabilitation programme. These patients usually have more-severe alcohol use disorders, little social support for abstinence, and unstable living conditions. In populations with drug and alcohol abuse, little evidence exists that different types of residential services have different outcomes. Cost and unavailability of facilities might restrict use of this option. Online treatment and telephone-based helplines have recently been trialled to increase treatment access for problem drinkers who are reluctant to seek traditional treatment. These treatments vary in content and delivery. Randomised controlled trials of internet-based treatment in college populations show large variations in response rates and retention. In alcohol-dependent populations, little evidence is currently available for telephone-based interventions or internet-based interventions. This rapidly developing area of research could, in future, deliver more effective online treatments for alcohol use disorders.
Public health policies are a cost-effective way to reduce the substantial population health burden that is attributable to alcohol intoxication—eg, policies that make alcohol more expensive by increase in taxation, and less accessible by restrictions on the sale and promotion of alcohol. These policies are also effective in reduction of the prevalence of alcohol use disorders.

Unresolved research questions

Preclinical and early clinical studies have investigated new drugs to treat alcohol use disorders. These drugs include selective antagonists (and agonists) of opioid, cannabinoid, nicotinic, neuropeptide, and dopaminergic receptors, and agents that modulate glutamate activity, glycine activity, the hypothalamic–pituitary–adrenal axis, and γ-aminobutyric-acid systems. On the basis of our review, drugs that have shown more consistent results but have not yet been approved for use include topiramate, gabapentin, baclofen, and varenicline (appendix).

Genetic factors could determine the effects of drugs and guide treatment selection, but the data are not sufficiently robust to justify routine clinical use of genetic tests. The Asn40Asp polymorphism of the opioid receptor, mu 1 (OPRM1) gene has been linked to effectiveness of naltrexone treatment in some but not all studies. The rs2832407 polymorphism in the GRIK1 gene, which encodes the kainate glutamate receptor subunit, could affect the effectiveness of topiramate treatment. High-quality replications are needed.

Research into health services is needed to better identify and treat the most common and remediable forms of psychiatric comorbidity in patients with alcohol use disorders—namely, anxiety and mood disorders. We need much better evidence to decide when treatment is needed for these psychiatric comorbidities and how best to integrate such treatment into the treatment of alcohol use disorders.

Conclusions

Alcohol use disorders contribute substantially to the burden of disease in many developed countries. Mild forms often remit without treatment, but the more severe forms are underdiagnosed and undertreated. The diagnosis and treatment of more-severe illness need to be improved—eg, doctors could screen patients in high-risk settings, reduce stigma, and engage patients earlier in effective psychological and pharmacological treatments. Ideally, patients should be offered a choice of behavioural or pharmacological treatments, or a combination of both. A pragmatic approach should be adopted towards patients who initially reject abstinence as a treatment goal.

Contributors

JPC, PSH, and WDH designed the content of the Seminar, conducted literature searches, drafted the Seminar and revised its content.

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JPC is supported by a National Health and Medical Research Council of Australia Career Development Fellowship (1031909). PSH is a member of the International Advisory Committee for
Lundbeck (nalmefene) and holds no shares or any financial interests. He has previously been a consultant for Alphapharm (acamprosate). WDH declares no competing interests.

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