

# Chapter 10. Comorbidities



## 10. Comorbidities

**This chapter provides an overview of treatment approaches to patients with alcohol-related physical comorbidity, co-occurring mental and alcohol use disorders, and people using multiple drugs, focusing on people who are polydrug dependent.**

### Physical comorbidity

Alcohol-related harm may result from the intoxicating effects of alcohol. Such harm largely relates to accidents and violence associated with the central nervous system depressant effects of alcohol. Adolescents are most at risk from:

- the long-term toxicity of alcohol on many organ systems, such as the liver, brain, heart, pancreas and peripheral nerves
- related lifestyle factors associated with chronic heavy alcohol use, such as poor nutrition.

Both short- and long-term regular heavy use can lead to psychosocial harms for individual drinkers.

The extent to which alcohol use contributes to organ damage varies considerably from person to person. Alcohol metabolism, nutritional deficiencies or excess, or immunological responses to the inflammation associated with alcohol mediated tissue injury, can all influence the extent of alcohol-related organ damage. While alcohol ingestion can clearly cause organ damage, it is also clear that some people can ingest large amounts of alcohol regularly over many years without any evidence of harm, suggesting considerable genetic variation; more research is needed to define the pathogenesis of alcohol-related organ damage. Conversely, some people appear unusually sensitive to end-organ damage, in some cases associated with other pathological processes.

Recommendation	Strength of recommendation	Level of evidence
10.1 Comprehensive assessment is indicated for patients with physical comorbidity related to alcohol, as multiple pathology is the rule.	A	I

The range of medical conditions affected by alcohol use is shown in Table 10.1. As it is beyond the scope of these guidelines to review the management of these conditions, readers should refer to relevant guidelines on managing particular conditions.

People who present with alcohol-related organ toxicity tend to experience less severe alcohol use disorders. People with chronic heavy alcohol use often have multiple medical, psychiatric and social problems and frequent 'crisis' presentations. Central to the approach to working with such people is:

- Thoroughly and systematically assessing alcohol and other drug use, physical, mental health, and social circumstances, using a biopsychosocial approach.
- Explaining clearly and factually the impact of the patient's alcohol use upon their health and social functioning.

- Developing a treatment care plan addressing alcohol and other drug use, and any related medical, mental health or social problems.
- Recommending abstinence for those with physical comorbidity related to alcohol unless mild and reversible pathology is present. In particular, pancreatitis may recur after a single drink.

Good communication between all agencies involved in assessing and managing such patients is imperative. The primary care worker (for example, general practitioner) is often well placed to coordinate various clinical teams involved with the patient, and to maintain long-term follow-up.

Recommendation	Strength of recommendation	Level of evidence
10.2 Abstinence is recommended for those with physical comorbidity related to alcohol unless mild and reversible pathology is present. In particular, pancreatitis may recur after a single drink.	D	IV
10.3 Comprehensive management requires a single practitioner with a broad range of clinical skills or close coordination between an appropriate team.	S	–

**Table 10.1: Alcohol use and physical complications**

Gastrointestinal	Liver disease, including alcohol-related fatty liver, alcoholic hepatitis, alcohol-related cirrhosis and multiple complications of cirrhosis and portal hypertension Liver cell cancer – hepatocellular carcinoma Acute and chronic pancreatitis Parotid enlargement Gastro-oesophageal reflux Peptic ulcer, gastritis, duodenitis Oesophageal rupture from violent vomiting bouts Small bowel damage leading to malabsorption Altered bowel habit with diarrhoea predominating
Cardiovascular	Hypertension High output cardiac failure Cardiomyopathy Acute rhythm disturbances in alcohol intoxication Coronary artery disease
Neurological	Cortical atrophy Cerebellar damage (midline structures maximally affected) Peripheral neuropathy Autonomic neuropathy Wernicke's encephalopathy Wernicke–Korsakoff syndrome Central pontine myelinolysis Marchiafava–Bignami syndrome Myopathy Cerebrovascular accidents Withdrawal delirium and neuronal damage
Musculoskeletal	Rhabdomyolysis Compartment syndromes Gout Osteopaenia Osteonecrosis

Haematological	Thrombocytopaenia from bone marrow suppression Pancytopaenia from hypersplenism Haemolytic anaemia with advanced liver disease - spur cell anaemia Macrocytic anaemia Folate and B12 deficiency anaemias Coagulopathies from liver disease
Immunological	Impaired B and T cell function mediated by alcohol toxicity Autoimmune phenomena triggered by acetaldehyde adducts acting as immunogenic targets IgA nephropathy
Respiratory	Increased predisposition to respiratory infection TB as a common infection Aspiration pneumonia Sleep apnoea
Endocrine	Syndrome of inappropriate antidiuretic hormone secretion (SIADH) Altered thyroid function Altered oestrogen metabolism associated with liver damage Masculinisation in women Pseudo Cushing's disease Altered calcium and bone metabolism Hypoglycaemia Aggravation of diabetes mellitus Ketoacidosis Hypertriglyceridaemia Testicular atrophy Hypoparathyroidism
Renal	IgA nephropathy
Infectious diseases	Hepatitis C virus Pneumonia Tuberculosis Sexually transmitted diseases
Nutritional disorders	Vitamin and mineral deficiencies; B1, B6, riboflavin, niacin, calcium, phosphate, zinc, magnesium. Protein calorie malnutrition
<b>Alcohol and malignancy</b>	The risk of developing certain malignancies increases from base risk levels with any alcohol consumption. These include breast, oropharyngeal and oesophageal cancers. Other malignancies such as colon, pancreatic, hepatic and ovarian are more prevalent in those drinking more than 40 gm per day.

## Co-occurring mental and alcohol-use disorders<sup>1</sup>

Co-occurrence of mental and alcohol use disorders presents special challenges in the treatment of people with alcohol problems.

Comorbid mental disorders are common among patients with alcohol problems. In Australia, of the 8841 people surveyed in 2007 for the National Survey of Mental Health and Wellbeing, 2.9 per cent met the criteria for alcohol abuse, and 1.4 per cent met the criteria for alcohol dependence. Of this latter group half (53.6%) met the criteria for an anxiety disorder and one-third (34.0%) met the criteria for an affective or mood disorder (ABS 2008). Other disorders associated with alcohol dependence include other substance use disorders. Equally, among people with mental disorders, such as depression, 34 per cent of men and 15 per cent of women have concurrent alcohol use problems. Approximately one in five patients with schizophrenia will have an alcohol use disorder at some time in his or her life.

<sup>1</sup> The recommendations in this section should be read in conjunction with clinical practice guidelines for the separate disorders (see Appendix 8 for a list).

In discussing comorbid mental disorders, this section uses the terminology of the fourth edition of the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV-TR: American Psychiatric Association 2000) because it provides specific criteria that define each disorder.

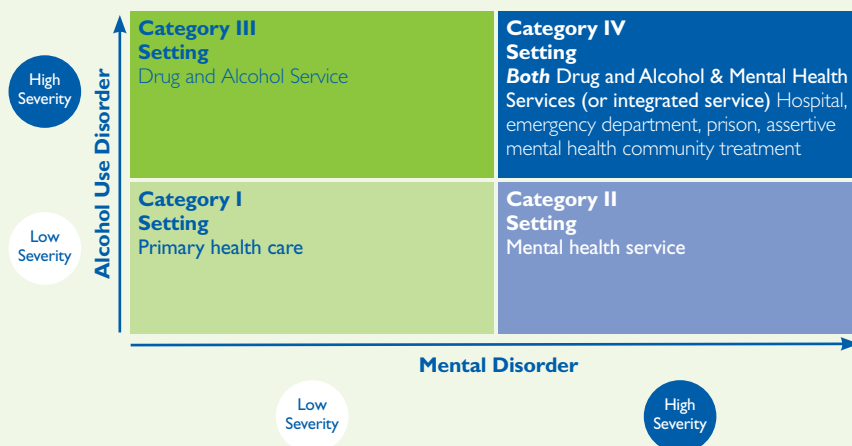
Comorbidity presents diagnostic dilemmas. Some co-occurrence appears to be a direct or withdrawal effect of alcohol, which remits with abstinence of at least 3 weeks duration. In other cases mental disorders are in parallel with alcohol use disorders. Still further cases show signs of mental disorders and alcohol interacting to cause greater problem severity, disability and poorer response to treatment. In addition mental disorders may emerge in early abstinence.

Patients with comorbid disorders of alcohol use and persisting mental comorbidity should be offered treatment for both disorders. Interventions for comorbid patients should be more intensive, as this population tends to be more disabled and carries a worse prognosis than those with single pathology.

Specialist services for people with alcohol problems need expertise in the assessment and treatment of comorbid mental disorders. While there is no direct clinical trial evidence for this recommendation, comorbidity is sufficiently common to justify integration of specialist drug and alcohol and mental health services. Patients referred from one service to another sometimes fail to take up the referral, and different services sometimes have different criteria for eligibility. Thus, to ensure the continuity of services, it is desirable to bring mental health expertise into alcohol treatment services rather than expecting patients to cope with geographic, administrative and clinical differences between services. Integration of the content of treatment is discussed in following sections.

Figure 10.1 illustrates the levels of integration of specialist drug and alcohol and mental health services. Depending on the relative severity of the patient's alcohol use disorder and mental disorder, the patient may receive care in an appropriate specialised setting or in a primary care setting.

**Figure 10.1: Level of care quadrants**



Source: Adapted from Center for Substance Abuse Treatment 2005, *Substance abuse treatment for persons with co-occurring disorders*, Treatment Improvement Protocol (TIP) Series 42, DHHS publication no. (SMA) 05-3922, Substance Abuse and Mental Health Services Administration, Rockville MD.

Recommendation	Strength of recommendation	Level of evidence
10.4 Patients with comorbid disorders of alcohol use and persisting mental health comorbidity should be offered treatment for both disorders.	A	Ib
10.5 More intensive interventions are needed for comorbid patients, as this population tends to be more disabled and carries a worse prognosis than those with single pathology.	B	I

## Assessment and diagnosis

Assessment for comorbid mental disorders and symptoms should form part of standard assessment procedures (see Chapter 3).

It is essential that assessment of particularly common problems such as anxiety and depression is a routine part of assessment. A key issue in assessment of co-occurring mental disorders is whether they are an effect of alcohol or a separate comorbid disorder. For example, the acute effects of alcohol or withdrawal from alcohol can cause symptoms of anxiety and depression. A period of abstinence is the most widely used way to make a differential diagnosis.

A first step in assessment of comorbid alcohol and mental disorders is consideration of the separate problems and their severity. Milder symptoms of anxiety and depression may not need separate attention but more severe forms may change the focus and setting of treatment. The Kessler 10 Symptom Scale is a scale of psychological distress widely used in Australia by general practitioners and mental health workers that appears suitable for monitoring and as an outcome measure in people with anxiety and depressive disorders.

The AUDIT appears to be a suitable screening tool for identifying risky, problem and dependent alcohol consumption among psychiatric patients. The ASSIST questionnaire can be used in mental health services to assess use of and problems with substances.

An important step in managing co-occurring mental disorders for those with alcohol dependence is to achieve a period of abstinence lasting 3 weeks or more. Abstinence for 3 to 6 weeks may help to show which anxiety and depressive disorders are comorbid and require their own treatment. If attempts to achieve short-term abstinence are not successful, an integrated approach may be appropriate as would be a greater emphasis on management of the co-occurring symptoms of mental disorder.

Among the anxiety disorders, agoraphobia and social phobia often predate the onset of drinking, which may be an attempt to control the symptoms. In contrast, panic disorder and generalised anxiety disorder often show onset after initiation of drinking and may be the effect of alcohol rather than a comorbid disorder. In addition some early epidemiological data suggested that social phobia, but not panic disorder, can begin before alcohol consumption and may have a distinct genetic vulnerability.

Comorbid mood and anxiety disorders, which do not abate after a period of abstinence, should be treated with integrated/concurrent cognitive behavioural therapy for the comorbid disorder (see Treatment below).

Recommendation	Strength of recommendation	Level of evidence
10.6 AUDIT is recommended for screening psychiatric populations.	A	Ib
10.7 Assessment for comorbid disorders should take place once the patient's withdrawal syndrome has diminished, since some anxiety and depressive symptoms may abate once alcohol consumption is reduced or ceased.	B	II

## Treatment

Co-occurring mental and alcohol use disorders should be managed in parallel with evidence-based treatments provided for both problems.

Comorbid mental disorders that do not abate within 3 to 6 weeks of abstinence (or significantly reduced drinking) or that emerge from such a period should be treated according to the clinical practice guidelines for those specific disorders.

Limited evidence supports integrating the content of treatment. Patient engagement in treatment planning and goal setting is particularly important in this population of patients. Adequate duration of treatment is essential to successful outcome. Clinicians should emphasise the patient's education and rising awareness of the interaction between alcohol use and symptoms of mental disorder. Patients with comorbid mood and alcohol use disorder should be regularly assessed and monitored for risk of suicide.

Little controlled research has been conducted to evaluate the effectiveness of treatment for comorbid patients, despite the knowledge that a sizeable proportion of alcohol dependent patients have a comorbid mental disorder. Several clinical trials show that typical pharmacological and psychological treatments for anxiety and mood disorders are effective in reducing anxiety and depression when they co-occur with alcohol use disorders. However, few controlled trials show that treating a comorbid mental disorder leads to reductions in drinking or delays relapse.

Recommendation	Strength of recommendation	Level of evidence
10.8 Comorbid mood and anxiety disorders that do not abate within 3 to 6 weeks after alcohol withdrawal is complete should be treated with integrated/concurrent cognitive behavioural therapy for the comorbid disorder.	B	II

## Psychosocial interventions

Comorbid mental disorders that last beyond a 3 to 6 week period of abstinence (or significantly reduced drinking) or that emerge from such a period should be treated according to the clinical practice guidelines for those specific disorders. The service that provides care should be integrated, but little evidence supports use of specific packages that integrate the content of psychological interventions.

Some considerations are:

- Where possible the same health professional should provide treatment for both alcohol use and comorbid disorders.
- Any combination of specific techniques should take care not to confuse the patient. It may be that in severely alcohol-dependent patients a focus on anxiety and depression may divert attention from reducing alcohol consumption early in treatment.

Specific psychological interventions that have strong empirical support for treating non-comorbid mental disorders are cognitive behavioural therapy, behaviour therapy, cognitive therapy, and interpersonal therapy. Other psychotherapies may be effective but there is to date insufficient evidence to recommend their use.

### **Anxiety disorders**

A recent meta-analysis summarised a disparate group of clinical trials and conclude there was no benefit in providing integrated psychological interventions for comorbid alcohol use and anxiety disorders. Some integrated interventions may produce better anxiety outcomes than interventions focused on alcohol but they may also produce worse results than focusing on alcohol alone.

Some evidence shows that the specific techniques of cognitive behavioural therapy, such as exposure to feared situations, is well tolerated by patients with substance use disorders, does not lead to relapse to drug use, and indeed contributes to reductions in anxiety.

### **Depression**

Some benefit for a disparate collection of integrated cognitive behavioural therapy programs for comorbid major depression and alcohol use disorders compared to a focus on alcohol alone was found in a recent meta-analysis. The specific cognitive behavioural therapy packages were described such as Behavioural Activation, Cognitive Therapy and Interpersonal Therapy.

### **Psychosis**

When managing patients with alcohol use disorders and severe mental disorders, such as psychoses, no compelling evidence supports one psychosocial treatment over another to reduce substance use or improve mental state. The Cochrane review of intervention treatment programs for people with both severe mental disorder and substance misuse, including alcohol, suggests that the evidence is poor at best with very few studies available for analysis. However, one trial demonstrated effectiveness of motivational interviewing in increasing abstinence from alcohol in this population.

Cognitive behavioural therapy also appears to be effective in treating those with comorbid psychoses. For example, integrating motivational interviewing, cognitive behavioural therapy and family intervention with routine psychiatric care has been shown to produce greater benefits for patients with comorbid schizophrenia and substance use disorders than routine psychiatric care alone. Typical benefits have included better general functioning, a reduction in positive symptoms, and an increase in the percentage of days abstinent from alcohol or drugs.

Integrating the psychosocial treatment for the mental disorder with the psychosocial treatment for alcohol use disorder may be beneficial in treatment of patients with such comorbidity. Relapse prevention strategies should take into account triggers for both alcohol use and mental disorders.

Recommendation	Strength of recommendation	Level of evidence
10.9 Cognitive behavioural therapy, behaviour therapy, cognitive therapy, and interpersonal therapy should be considered for treatment of patients with comorbid mental and alcohol use disorders because of their demonstrated effectiveness in non-comorbid cases.	B	Ib
10.10 Integrating psychosocial treatment for mood disorders and psychoses with psychosocial treatment for alcohol-use disorder may be beneficial in treating patients with such comorbidity.	D	IV

### Pharmacological treatment

Pharmacological treatments have proved effective in treating anxiety, depression and psychosis in patients exhibiting co-occurring mental and alcohol use disorders.

#### Anxiety

Typical pharmacological treatments for anxiety and mood disorders also reduce anxiety and depression when they co-occur with alcohol use disorders. However, treating only a comorbid mental disorder usually does not lead to a reduction of alcohol consumption.

Selective serotonin reuptake inhibitors (SSRIs) reduce symptoms of anxiety in patients with comorbid anxiety and alcohol dependence. They are indicated for treatment of obsessive-compulsive disorder and panic attacks in these patients. However, little sound evidence supports their capacity to reduce alcohol intake in the longer-term in patients with comorbid anxiety disorders.

Benzodiazepines are effective anxiolytics and are used in treatment of acute alcohol withdrawal but should not be used beyond this indication. They are not recommended in treatment of comorbid anxiety due to high risk of dependence and a potential synergistic interaction with alcohol.

Buspirone (an anxiolytic) in conjunction with psychosocial therapy is better than placebo in reducing both anxiety symptoms and alcohol consumption. In one study, patients taking buspirone were more likely to remain in treatment for the 12 weeks, had reduced anxiety, a slower return to heavy alcohol consumption, and fewer drinking days during the 6 months follow-up period.

Combining pharmacological and psychosocial interventions may be beneficial, particularly when psychosocial interventions for alcohol use disorders are integrated with those for anxiety.

#### Depression

Meta-analyses of randomised controlled trials indicate that antidepressant medication has a modest beneficial effect for patients with combined depressive and substance-use disorders. It is not recommended as a stand-alone treatment. Concurrent treatment directly targeting the addiction is also indicated. The findings also suggest a clinical approach that begins with an evidence-based psychosocial intervention, followed by antidepressant medication if depression does not improve.

Antidepressants may help relieve depressive symptoms but have little effect on reducing alcohol consumption, unless accompanied and supported by psychosocial treatment for alcohol-use disorder.

SSRIs reduce depressive symptoms in patients with comorbid major depression and alcohol dependence; however, research results regarding their effectiveness in reducing alcohol consumption in these patients are conflicting. SSRIs should not be used as primary therapy to reduce alcohol consumption in patients with comorbid depression.

Desipramine (a tricyclic antidepressant) has been shown to reduce relapse in alcohol dependent patients diagnosed with major depression, but not in those without major depression. Some noradrenergic antidepressants show promise for reducing relapse or drinking in comorbid patients. For example, nortriptyline (a noradrenergic antidepressant) reduces drinking in patients diagnosed with antisocial personality disorder, but not in those patients with affective/anxiety disorders or those without a comorbid disorder.

Tricyclic antidepressants should be used with caution in this population due to high risk of poor treatment adherence, abuse and overdose.

Antidepressants should not be the first line of treatment in patients with comorbid alcohol use disorders, unless there is high level of suicidal ideation, severe depressive symptoms or a history of pre-existing depressive illness. Clinicians should consider heavy drinkers' potential for poor treatment compliance. Psychological treatment options should be used first, integrating approaches that are aimed at reducing alcohol consumption with those targeting depressive symptoms.

### Psychosis

A qualified mental health practitioner usually provides pharmacological treatment of psychotic illness. Atypical antipsychotics appear to be the first line of treatment of comorbid psychotic illness and substance use disorders. Limited evidence shows that among schizophrenic patients, two atypical antipsychotics (risperidone and clozapine) may reduce alcohol misuse, smoking, and possibly some other substance misuse.

Addition of psychosocial support to pharmacological treatment has been shown to be effective in treatment of patients with comorbid psychosis and alcohol use disorders.

Clinicians should recognise the potential for poor medication adherence in heavy drinkers prescribed antipsychotic medications.

Recommendation	Strength of recommendation	Level of evidence
10.11 Selective serotonin reuptake inhibitor antidepressants are not recommended as primary therapy to reduce alcohol consumption in patients with comorbid mood or anxiety disorders.	B	II
10.12 Benzodiazepines are not recommended for treatment of comorbid anxiety in patients with alcohol-use disorders due to high risk of dependence and a potential synergistic interaction with alcohol.	S	–

### Polydrug use and dependence

Polydrug use has become commonplace in Australia. Most Australians who drink alcohol also use other drugs such as prescription medication (opioid analgesics, benzodiazepines) or illicit drugs (cannabis, amphetamines, cocaine, ecstasy).

In Australia, among those people with alcohol use disorders, 51 per cent of those who were alcohol-dependent were regular tobacco smokers, 32 per cent had used cannabis, 15 per

cent reported other drug use, 15 per cent met the criteria for a cannabis use disorder, and 7 per cent met the criteria for another drug use disorder (Degenhardt 2003). Reasons for polydrug use include:

- combined drug effects (for example, to enhance intoxication by combining alcohol and benzodiazepines)
- to counter the effects of other drugs (for example, using a sedative such as alcohol to counter the effects of stimulants)
- use of a drug in lieu of other drug use (for example, benzodiazepines to compensate for lack of alcohol)
- dependence on multiple drugs.

Dependence on multiple drugs refers to polydrug dependence. Polydrug dependence is typically associated with greater severity of dependence, higher levels of psychiatric and physical comorbidity, greater treatment resistance with poorer clinical outcomes, and often more complicated and severe withdrawal syndromes. This is especially the case for people who have concurrent dependence upon alcohol and benzodiazepines, where withdrawal is typically more severe and protracted, requiring higher doses of medication.

Although many patients with alcohol and comorbid other substance use disorders may only see one substance as a problem, their use of other substances will often need to be addressed in order to achieve a successful outcome with respect to their primary substance of concern. It is important to address polydrug use when treating alcohol use disorders because:

- Ongoing use of other drugs by drinkers may reduce the efficacy of both psychological and pharmacological interventions, and is often associated with poorer engagement and retention in treatment.
- Polydrug use can exert significant effects upon the time course and severity of alcohol withdrawal. Early detection of other drug use and risks of withdrawal from multiple drugs may avoid potentially severe complications during withdrawal. For polydrug dependent people seeking treatment, a stepped approach to detoxification (addressing management of one withdrawal syndrome at a time) is often preferable though not always practical.
- Clinicians and patients should be aware that cessation of alcohol use may lead to changes in the pattern of other substance use. In some cases these changes may be positive, especially where alcohol use may play a priming role in the use of the other substance, such as cocaine or tobacco. In other cases it may be that a reduction in alcohol use may lead to increased use of other substances. Uptake of other sedative drugs (benzodiazepines, cannabis) is most common following alcohol cessation, and may be short-term (in an attempt to manage alcohol withdrawal symptoms), but may become a longer-standing issue, especially where untreated psychiatric comorbidity (such as anxiety, depression) is present. Given the pharmacological effects and common use of benzodiazepines in managing alcohol withdrawal, the potential for increased benzodiazepine use and dependence needs particular attention. Conversely, cessation of the other drug use (such as opioids, benzodiazepines) may lead to increased alcohol consumption.

Patients should be informed of the potential impact of alcohol cessation upon other drug use. Use of other drugs should be monitored during follow-up, and patients should be provided with a range of coping strategies (sleep habits, relaxation and anxiety management techniques) to minimise their risk of developing dependence on other drugs.

## Screening, assessment and treatment planning

The most common comorbidity of people diagnosed with alcohol dependence is another substance use disorder; such disorders occur seven times more frequently in this population than in the general population. The most common comorbid substance dependencies for people with alcohol dependence, other than nicotine, are other depressants (such as benzodiazepines, cannabis, opioids) and stimulants (such as cocaine). This means people presenting with alcohol use disorders must also be screened for other substance use disorders.

Quantity–frequency estimates of alcohol and other drug use must consider that use of alcohol is often related to other drug use; a person may increase their use of benzodiazepines when alcohol is not available. Clinicians need to gather a comprehensive history in order to assess the variation in drug use (see Chapter 3). Using validated screening instruments for multiple drugs (such as ASSIST: see Appendix 1) can be incorporated into screening approaches.

The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) is a screening questionnaire recommended by the World Health Organization. It is designed to detect substance use and related problems in primary and general medical care settings. ASSIST provides a valid measure of substance-related risk both for individual substances and for total substance use involvement. The test can distinguish between people who:

- are low risk substance users or abstainers
- have developed or are at risk of developing problems and/or at risk of developing dependence
- are dependent on a substance.

Clinicians should also assess the related harms and increased risk of comorbidities arising from polydrug use. These include:

- **Alcohol and central nervous system depressants: opioids, benzodiazepines, prescription drugs, GHB.** The combined use of alcohol and other depressant drugs (such as benzodiazepines, opioids, GHB; and/or sedating medications such as tricyclic antidepressants) increases the risk of impaired cognition, driving and work performance. Alcohol also enhances central and respiratory depressant effects of such drugs, potentially causing respiratory depression, coma and overdose death. Alcohol also impairs risk assessment and memory, thereby hindering the ability to safely titrate doses of other drugs, again increasing the risk of short-term harms (such as driving accidents, overdose).
- **Alcohol and stimulant drugs: cocaine, amphetamines and MDMA (also known as ecstasy).** Alcohol is commonly used in combination with stimulant drugs. Combined use increases the risks of dehydration, thermal dysregulation, cardiac toxicity, sleep and mental health problems (such as psychosis, anxiety, depression).
- **Alcohol and cannabis.** Alcohol has synergistic effects with cannabis, markedly increasing the cognitive and psychomotor impairment seen with each substance. The combined use of alcohol and cannabis can be dangerous when engaging in any activity requiring motor skills and judgement (such as driving a motor vehicle). Both cannabis and alcohol can significantly contribute to mental health problems (such as psychosis, anxiety, depression).

Recommendation	Strength of recommendation	Level of evidence
10.13 All patients with alcohol-use disorders should be screened for other substance use using quantity–frequency estimates, or through structured screening instruments such as the ASSIST questionnaire.	D	IV
10.14 Polydrug dependence is typically associated with higher levels of physical, psychiatric and psychosocial comorbidity that should be addressed in comprehensive treatment plans.	D	IV
10.15 Use of other drugs can be affected by cessation or reduction in alcohol use, and treatment plans should address use of alcohol and other drugs together.	D	IV

### Polydrug withdrawal

Polydrug withdrawal refers to the situation that arises where a person physically dependent on more than one substance ceases or significantly reduces their consumption of those substances and experiences withdrawal syndromes from more than one drug class.

Typically, withdrawal from more than one substance, in addition to alcohol, can affect the course of withdrawal in a number of ways. Many different drug withdrawal syndromes have considerable overlap in symptoms, reflecting common withdrawal changes in autonomic arousal (restlessness, elevated blood pressure, tachycardia, sweating, abdominal symptoms), mood (anxiety, dysphoria), sleep and cravings. This overlap can:

- increase severity of withdrawal and risk of withdrawal complications, such as dehydration, seizures, severe agitation, hallucinations or delirium; for example, concomitant withdrawal from alcohol and short-acting benzodiazepines like alprazolam or temazepam is likely to increase the risk of seizures and withdrawal from alcohol and opiates is likely to increase the risk of dehydration
- change the onset and duration of withdrawal; for example, stopping alcohol and long-acting benzodiazepine use may delay the onset of withdrawal symptoms and complications, such as seizures or delirium.

### Managing polydrug withdrawal

Because of the potential for unexpected withdrawal severity, onset or duration, and the increased risk of withdrawal complications, clinicians should closely monitor and supervise patients undergoing withdrawal from multiple drugs. This will often require an inpatient (detoxification unit or hospital) setting.

The overlap of symptoms can complicate assessment and monitoring of withdrawal syndrome. As such alcohol or other drug withdrawal scales (such as CIWA-Ar, AWS) require careful interpretation, and should not generally be used for symptom-triggered medication regimens (such as the symptom-triggered diazepam regimen for alcohol withdrawal; see Chapter 5). Fixed diazepam dosing regimens are preferred for managing alcohol withdrawal in the context of other drug withdrawal. Clinicians need to regularly review medication regimens.

Clinicians should carefully consider the order in which withdrawal from different drugs should be managed. The driving principle in determining the order of detoxification in a polydrug dependent person is to prioritise the substance with the potential for the most problematic withdrawal. In most instances, therefore, alcohol will be the first drug from which to support withdrawal. Wherever possible, withdrawal from other drugs can be prevented or minimised by:

- using substitution medications (such as methadone or buprenorphine for opioid dependence, diazepam for benzodiazepine dependence, and nicotine replacement for tobacco dependence)
- allowing resolution of alcohol withdrawal before attempting withdrawal from other medications (with, for example, methadone or diazepam dose reduction).

This typically prolongs withdrawal. Alternatively, the treatment plan may involve longer-term stabilisation on the substitution medication (for example, methadone maintenance treatment). Table 10.2 provides information on specific polydrug withdrawal combinations and treatment plans.

Substitution medications are not available or routinely used for some polydrug combinations (such as cocaine, amphetamine, cannabis withdrawal). As well, withdrawal may be attempted in settings where substitution medications may not be readily available (such as custodial settings). Under these circumstances, patients may experience greater levels of withdrawal severity, such as agitation and sleep disturbance, that need close monitoring, increased supportive care, and increased doses of medication than would be routinely used for single drug withdrawal management.

It is important to discuss treatment plans with patients so they understand what is happening (for example, clarification that the dose of methadone will remain stable during withdrawal from alcohol). Negotiate with patients over the choice of medication. Some patients dependent upon short-acting benzodiazepines (such as alprazolam or oxazepam) may not be confident that diazepam will be efficacious in their withdrawal from both their benzodiazepine of choice and alcohol. Clinicians should regularly inform patients and carers about the likely course and nature of withdrawal symptoms.

It is important when managing polydrug withdrawal that clinicians set clear and consistent boundaries with patients who exhibit drug-seeking behaviours.

**Table 10.2: Clinical profile and treatment plans for withdrawal from alcohol and other drugs**

Alcohol + opiates	Alcohol + stimulants	Alcohol + cannabis	Alcohol + benzodiazepines
<b>Clinical profile</b>			
Alcohol use is common among opiate users and increases risk for those with hepatitis C infection. Combined withdrawal may result in increased sympathetic stimulation increased dehydration, sleep, mood and gastrointestinal disturbances.	The combined use of alcohol and stimulant drugs often leads to high levels of consumption of both drugs. Alcohol may be used to induce insomnia and relaxation in stimulant users.  More severe and protracted withdrawal may be expected, related to consumption and anorexia.	Some users report using cannabis to self-medicate anxiety or insomnia linked to alcohol withdrawal.  Combined withdrawal is likely to be associated with increased mood and behavioural disturbance.	Both substances modulate GABA function; simultaneous withdrawal can increase symptom severity and risk of seizures. The more protracted withdrawal syndrome associated with benzodiazepines may delay onset of withdrawal symptoms, and prolong withdrawal.
<b>Treatment plan</b>			
Consider stabilisation on buprenorphine or methadone while undergoing alcohol withdrawal.  Higher benzodiazepine (diazepam) doses may be needed in lieu of opioid substitution.	Higher doses of benzodiazepines (diazepam) may be needed.	Higher doses of benzodiazepines (diazepam) may be needed.	Dependent alcohol and benzodiazepine users will need higher doses of diazepam, and consider a gradual diazepam taper.

Note: All clinicians should be advised when, where and who to go to for further advice.

Recommendation	Strength of recommendation	Level of evidence
10.16 Patients undergoing polydrug withdrawal need close monitoring, increased psychosocial care, and increased medication. Consider specialist advice.	D	IV
10.17 Fixed diazepam dosing regimens are preferred for managing alcohol withdrawal in the context of other drug withdrawal, with regular review of the dosing regimen. Withdrawal scales (such as CIWA-Ar) need careful interpretation in patients withdrawing from multiple drugs, and should not be used to direct medication.	D	IV
10.18 Patients dependent on alcohol and benzodiazepines or opioids should be stabilised on substitution medications while undergoing alcohol withdrawal.	D	IV