

6 Anxiety disorders and substance use

6.1 Anxiety

In contrast to fear, which is a response to a realistic immediate danger, anxiety is a fearful response occurring in the absence of a specific danger or real threat. According to the National Survey of Mental Health and Wellbeing, anxiety disorders are the most common form of mental disorder in the population with a one-year prevalence of 9.7% in Australian adults⁽⁶⁸⁾.

The fear and worry associated with anxiety arises in response to a variety of specific triggers (fear of heights) more general triggers (e.g. crowds, shopping centres, being in trains or buses, meeting new people, or having to speak in public) or sometimes in response to general issues including finances, health or relationships and personal safety. In some cases, anxiety can arise suddenly and spontaneously without a discernable trigger, as is the case with panic disorder.

People with anxiety may find it hard to relax, concentrate and sleep, and may suffer physical symptoms such as heart palpitations, tension and muscle pain, sweating, hyperventilation, dizziness, faintness, headaches, nausea, indigestion, bowel disturbance and loss of sexual pleasure. These symptoms are accompanied by changes in thoughts, emotions and behaviour that substantially interfere with the person's ability to live and work.

More women than men experience anxiety disorders^(68, 119, 121, 201). Anxiety usually begins in early adulthood and is often, but not always, triggered by a series of significant life events.

6.1.1 Anxiety disorder subtypes

Panic disorder

- This is characterised by recurrent panic attacks, which occur unexpectedly over at least a month. Panic attacks are diagnosed if there is a period in which there is a sudden onset of intense apprehension, fearfulness or terror commonly associated with feelings of impending doom. Symptoms such as shortness of breath, palpitations, chest pain or discomfort, smothering or choking sensations along with fear of losing control are experienced during these attacks.

Agoraphobia

- This is characterised by anxiety about, or avoidance of, places and situations from which escape may be difficult (e.g. elevators, buses, trains or trams or shopping centres), or in which help may not be available in the instance of experiencing a panic attack or panic like symptoms.

Social phobia

- This is characterised by clinically significant anxiety provoked by being exposed to certain types of social situations, commonly leading to avoidance of situations requiring socialising.

Obsessive compulsive disorder (OCD)

- This is characterised by obsessions that cause significant anxiety or distress and compulsions which serve to neutralise the associated anxiety or distress.

Post traumatic stress disorder (PTSD)

- This is characterised by re-experiencing of an extremely traumatic event accompanied by symptoms of increased arousal and avoidance of stimuli associated with the trauma.

Generalised anxiety disorder (GAD)

- This is characterised by at least six months of persistent and excessive anxiety or worry.

6.1.2 Management approaches to anxiety disorders

- Anxiety disorders are treatable conditions, although as with all medical disorders, there is a spectrum of severity. Some are chronic. Anxiety disorders have a generally unappreciated high rate of morbidity and mortality⁽¹⁹⁶⁾.
- Discussions with the patient regarding treatment should involve both short- and long-term outcome goals⁽¹⁹⁶⁾.
- Treatment of the anxiety disorders vary depending on the nature of the condition and the circumstances of the individual. In most cases, CBT is first-line treatment^{****(202)} and is cheaper and more effective than medication, especially in those individuals who have had little or no previous exposure to benzodiazepines.
- In the majority of situations, however, by the time people seek advice from a clinician they are not generally benzodiazepine naïve and the issue expands to management of anxiety as well as controlling benzodiazepine use.
- Patients taking benzodiazepines do not develop tolerance to their anxiolytic effects⁽¹⁹⁶⁾ which significantly contributes to the desire to continue with their use. Benzodiazepines are particularly best avoided as a long-term medication treatment in the elderly because of the risk of adverse effects.
- CBT is effective in reducing symptoms of anxiety^{****(202)} and will be more effective if there is minimal sedation and anxiolysis due to benzodiazepine use⁽¹⁹⁶⁾.
- However, CBT can be and is effective when administered concurrently with benzodiazepine dose reductions^{****(202-204)}. CBT has been shown to improve the likelihood of patients successfully tapering and ceasing benzodiazepine use when they also have an anxiety disorder^{****(204)}.
- Tricyclic antidepressants and SSRIs are equally effective and preferable to benzodiazepines because of problems with sedation and associated dependence and withdrawal.
- People with social phobias may show some treatment response with antidepressants, in particular SSRIs^{****(205-213)}. People with OCD also respond well but require higher than normal doses⁽²¹⁴⁻²¹⁸⁾.
- Benzodiazepines may be more useful than antidepressants for GAD, panic disorder and agoraphobia^{*(196)}. However, both anti-depressants and/or benzodiazepines should only be used after other treatment approaches have been unsuccessful. That is, they should only be used as a third or fourth line of treatment when patient responses to other forms of management have been unsuccessful.

6.2 Comorbidity with anxiety disorders

- Anxiety frequently occurs in conjunction with other mental disorders, in particularly depression^(10, 28, 58, 68, 123, 201, 219-224).
- Anxiety has also been shown to co-occur frequently with suicidality^(28, 219) and somatisation disorders⁽¹²³⁾.
- The presence of anxiety as a comorbidity increases the level of impairment associated with the primary disorder^(58, 123).
- Anxiety (particularly PTSD) is commonly seen in association with substance use^(10, 11, 23, 28, 29, 68, 121, 196, 221, 224).
- The causal relationship between anxiety disorders and substance use (self-medication theories, substance-induced anxiety) are not clearly established⁽¹⁹⁶⁾.
- Anxiety is also a common feature of substance withdrawal^(46, 194, 196).

6.3 Major clinical issues with anxiety disorders and cannabis/hallucinogen use

- Cannabis can induce anxiety or panic attacks especially in naïve users.
- In chronic users, cannabis tends to have the opposite effect and act more as an anxiolytic at the time of use.
- Individuals should be encouraged to reduce or cease using so that anxiety symptoms can be better evaluated. In many cases this will result in an overall reduction in anxiety symptoms once withdrawal has passed.
- Cannabis withdrawal commonly includes insomnia which can be prolonged. The longer term use of hypnotics to assist with sleeping is problematic due to tolerance development.
- In the absence of other proven forms of treatment, CBT is, at present, the most widely employed form of treatment for cannabis use.

6.3.1 Effects of cannabis and other hallucinogens on anxiety disorders

- Anxiety is common in people who use cannabis and other hallucinogens, particularly for those who commenced use at a young age⁽⁶⁻¹³⁾.
- Heavier or more frequent use of cannabis is a greater predictor of anxiety^(6, 9, 12, 13).
- Cannabis can induce anxiety or panic attacks^(6, 12, 13, 225) especially in naïve users.
- In chronic users, cannabis tends to have the opposite effect and act more as an anxiolytic at the time of use.
- It is also thought that anxiety may predispose people to cannabis use problems^(7, 8).

6.3.2 Interactions between *cannabis and other hallucinogens and therapeutic agents for anxiety disorders*

- Cannabis can exacerbate the sedative effects of tricyclic antidepressants and benzodiazepines, which increases the risk of impaired driving and injury as well as overdose[✖].
- LSD may induce a serotonin syndrome (Appendix 1); therefore caution should be exercised when prescribing SSRIs or MAO-I^{✖(127)}.
- Cannabis and antidepressants are metabolised by CYP 450 enzymes which may result in the inhibition or induction of either drug group. Therefore, individuals should be monitored closely to follow clinical response and to ensure that toxicity does not occur[✖].

6.3.3 Management approaches to comorbid anxiety disorders and *cannabis use*

- Cannabis can induce anxiety symptoms, particularly in first time users. The effect is dose related. In addition, anxiety is a feature of cannabis withdrawal. People should be encouraged to reduce or cease using so that anxiety symptoms can be better evaluated. In many cases this will result in an overall reduction in anxiety symptoms once withdrawal has passed.
- Abstinence from cannabis is a difficult goal to achieve in cannabis dependent people⁽¹²⁸⁾.
- In the absence of other proven forms of treatment, CBT is, at present, the most widely employed form of treatment for cannabis use^{****(128)}.
- CBT is effective in reducing symptoms of anxiety^{***(196, 203)}. CBT that focuses on coping mechanisms will be most effective if the individual has been using cannabis or other hallucinogens to self-medicate and cope with social anxiety situations.
- Treatment of acute anxiety associated with cannabis withdrawal can be treated with benzodiazepines; however, use should be minimised as those with substance use disorders are at a greater risk of abusing benzodiazepines⁽¹⁹⁶⁾.
- Cannabis withdrawal commonly includes insomnia which can be prolonged. The longer term use of hypnotics to assist with sleeping is problematic due to tolerance development⁽¹⁸⁸⁾.
- Psychological and behavioural treatment can be effective in treating insomnia^{***(190-192)} associated with psychiatric disorders⁽¹⁹³⁾ and may reduce the need for benzodiazepine use during depression.

6.4 Major clinical issues with anxiety disorders and alcohol use

- Alcohol use and anxiety disorders frequently co-occur and exacerbate each other.
- Individuals should be encouraged to reduce or cease alcohol use so that anxiety symptoms can be better evaluated.
- Anxiety associated with alcohol withdrawal should be allowed to subside, before making a diagnosis of anxiety disorder.
- However, anxiety may be a feature of the post-withdrawal state lasting for several months (up to 12 months).
- SSRIs are also effective in alcohol dependent people with anxiety.
- CBT should be given prior consideration over benzodiazepine therapy.
- Disulfiram, naltrexone and acamprosate used to treat alcohol dependence are unlikely to interact with antidepressants if these are being used.
- Acamprosate, naltrexone and benzodiazepines do not appear to interact with one another.
- Successful treatment of either anxiety or alcohol use disorder with CBT does not necessarily result in a positive outcome for the accompanying comorbid disorder.
- Pharmacotherapies such as naltrexone, acamprosate and disulfiram are effective in the management of alcohol dependence and maintaining abstinence and are effective in individuals with comorbid anxiety.

Alcohol

6.4.1 Effects of alcohol on anxiety disorders

- Alcohol use and anxiety disorders frequently co-occur^(10, 18-23).
- Problematic alcohol use and anxiety exacerbate each other, leading to increased severity of both the anxiety disorder and alcohol use⁽²²⁶⁾.
- The short-term relief in symptoms that alcohol gives people with anxiety is a strong motivator for continued alcohol use^(10, 18, 22, 226).
- However, as dependence develops, this ultimately leads to increased anxiety:
 - Alcohol withdrawal produces anxiety.
 - Excessive alcohol use can result in environmental situations or disruptions that cause anxiety⁽²²⁶⁾.
- Higher anxiety sensitivity (people with increased levels of sensitivity to anxiety who do not have a diagnosable anxiety disorder) is highly predictive of alcohol use disorders⁽²²⁷⁾.
- Higher levels of anxiety are more indicative of relapse to drinking alcohol⁽²²⁸⁾.

6.4.2 Interactions between alcohol and therapeutic agents for anxiety disorders

- Alcohol can exacerbate the sedative effects of any sedative agents (including tricyclic antidepressants, mirtazepine, and benzodiazepines used in the treatment of anxiety[✖]).
- Alcohol toxicity may occur through:
 - The inhibition of CYPs by sedative antidepressant involved in the metabolism of alcohol^{✖(133)}.
 - An increase in sedation as a result of combinations of alcohol and benzodiazepines[✖].
- Disulfiram used to treat alcohol dependence will increase the plasma concentrations of diazepam leading to possible increases in sedation and overdose[✖].
- Disulfiram, naltrexone and acamprosate used to treat alcohol dependence are unlikely to interact with antidepressants if these are being used^{✖(229)}.
- Acamprosate, naltrexone and benzodiazepines do not appear to interact with one another^{✖(230)}.

6.4.3 Management approaches to comorbid anxiety disorders and alcohol use

- Due to the anxiety-provoking effect of alcohol, and vice versa, individuals should be encouraged to reduce or cease alcohol use so that anxiety symptoms can be better evaluated⁽²²⁶⁾.
- Clinicians should allow sufficient time for anxiety associated with alcohol withdrawal to subside, before making a diagnosis of anxiety disorder^(226, 231).
- However, anxiety may be a feature of the post-withdrawal state lasting for several months (up to 12 months).
- If large quantities of alcohol are being consumed, then inpatient withdrawal or detoxification with benzodiazepines should always be considered to avoid and manage seizure risk. Concerns about benzodiazepine dependence should not prevent controlled prescribing for withdrawal states.
- Benzodiazepine use should be monitored and minimised as those with substance use disorders are at a greater risk of abusing benzodiazepines⁽¹⁹⁶⁾.
- Successful treatment of either anxiety or alcohol use disorder with CBT does not necessarily result in a positive outcome for the accompanying comorbid disorder^{****(231)}. That is outcomes for the two sets of problems are somewhat independent. However, CBT can be effective in:
 - Improving alcohol-related outcomes in people with anxiety and alcohol dependence and is more effective in those who drink less^{****(226, 231, 232)}.
 - Reducing symptoms of anxiety^{****(196, 202)} in those with additional alcohol-related problems^{****(231)}. CBT should be given prior consideration over benzodiazepine therapy.
- SSRIs may be effective in reducing anxiety^{****(205-218)}.
- SSRIs are also effective in alcohol dependent people with anxiety^{****(233)} in situations where behavioural therapy is not possible or unsuccessful.
- Consistent with the situation with depression and alcohol dependence, SSRIs may even improve drinking outcomes in those with less severe alcohol dependence^(220, 234).

- However, some studies of SSRIs used to treat alcohol dependent people have shown a worsening effect on alcohol consumption in certain subtypes, in particular those with early onset problem drinking^{***(138, 139)} and therefore requires monitoring.
- Pharmacotherapies such as naltrexone, acamprostate and disulfiram are effective in the management of alcohol dependence and maintaining abstinence, and are effective in individuals with comorbid anxiety^{****(141, 144, 235-237)}.

6.5 Major clinical issues with anxiety disorders and opioid use

- While opioids do not possess anxiolytic effects in the manner that benzodiazepines do, they do have the ability to enable the person to forget about the issues that may be causing them to feel anxious. An indirect short-term reduction in symptoms of anxiety may be a strong motivator for opioid use in those with anxiety disorders.
- Methadone itself has been shown to inhibit CYP3A4 which also metabolises many benzodiazepines. This has the potential to increase plasma concentrations of benzodiazepines and increase their sedative effects.
- Several deaths have been reported due to benzodiazepine use in conjunction with high dose buprenorphine and may be a result of similar metabolic interactions.
- Fluvoxamine^{***}, fluoxetine^{**}, norfluoxetine^{**} and paroxetine^{*} can inhibit buprenorphine and methadone metabolism through inhibition of the CYPs involved in their metabolism.
- Citalopram and sertraline are the least likely SSRIs to have cytochrome mediated drug interactions.
- If long-term benzodiazepine use is unable to be avoided, this should be monitored very closely.
- Acute opioid withdrawal is best managed using buprenorphine.
- If treatment of anxiety with antidepressants is required, this should involve non-sedating antidepressants such as SSRIs, taking into consideration their interaction effects.
- Longer acting maintenance pharmacotherapies such as methadone and buprenorphine potentially stabilise opioid plasma concentrations and reduce fluctuations in plasma concentration and levels of anxiety.

Opioids

6.5.1 Effects of opioids on anxiety disorders

- Those with anxiety disorders are significantly more likely to use opioids than those without anxiety disorders^(11, 25, 28, 29).
- While opioids do not possess anxiolytic effects in the manner that benzodiazepines do, they do have the ability to enable the person to forget about the issues that may be causing them to feel anxious. An indirect short-term reduction in symptoms of anxiety may be a strong motivator for opioid use in those with anxiety disorders.

- People with anxiety disorders report more severe opioid dependency than those without anxiety⁽²⁸⁾.
- There is some debate as to whether anxiety can potentially have an adverse impact on the effectiveness of opioid maintenance pharmacotherapy^(238, 239).

6.5.2 Interactions between **opioids** and therapeutic agents for anxiety disorders

- Methadone itself has been shown to inhibit CYP3A4^{x x (240, 241)} which also metabolises many benzodiazepines. This has the potential to increase plasma concentrations of benzodiazepines and increase their sedative effect^{x (242, 243)}.
- Several deaths have been reported due to benzodiazepine use in conjunction with high dose buprenorphine and may be a result of similar metabolic interactions^{x x x (244-246)}.
- Fluvoxamine^{x x x}, fluoxetine^{x x}, norfluoxetine^{x x} and paroxetine^x can inhibit buprenorphine and methadone metabolism through inhibition of the CYPs involved in their metabolism⁽¹⁴⁸⁻¹⁵⁰⁾. This can result in an increase in plasma opioid pharmacotherapy concentrations and potential overdose. This can be a particular issue during induction onto methadone; however, the risk may persist even after stabilisation has occurred^{x x x (151-155)}.
- Fluvoxamine is the most potent inhibitor of methadone and buprenorphine metabolism and is the most clinically relevant. Therefore, it should be avoided^{x x x (150)}.
- Fluoxetine and paroxetine should also be avoided due to their possible effects on methadone metabolism^{x x}.
- Citalopram and sertraline are the least likely SSRIs to have cytochrome-mediated drug interactions; however, due to the theoretical potential for an interaction, caution should still be used and individuals monitored closely^{x (156)}.

6.5.3 Management approaches to comorbid anxiety disorders and **opioid use**

- Fluctuating plasma concentrations of short acting opioids such as heroin can exacerbate anxiety disorders due to the effects of withdrawal at times of low plasma concentration. Therefore, patients should be encouraged to reduce their use and, if possible, cease.
- Longer-acting maintenance pharmacotherapies such as methadone and buprenorphine potentially stabilise opioid plasma concentrations and reduce fluctuations in plasma concentration and levels of anxiety. However, relatively small changes in maintenance therapy concentrations can result in significant mood changes^{x (247)}.
- Acute opioid withdrawal is best managed using buprenorphine^{***x (248)}. However, benzodiazepines can be used if there is continuing residual anxiety. Their use should be minimised due to risk of misuse⁽¹⁹⁶⁾.
- If long-term benzodiazepine use cannot be avoided:
 - This should be subject to a contract with the patient.
 - Authorities should be advised, including registration with the relevant local government health authority.
 - The seeking of additional benzodiazepines from other prescribers should be monitored (e.g. using the *Authority to release personal PBS claims information to a third party form*).

- Daily or weekly dispensing of benzodiazepines in conjunction with collection of methadone or buprenorphine doses should be considered and may assist with controlling use.
- If treatment of anxiety with antidepressants is required, this should involve non-sedating antidepressants such as SSRIs, taking into consideration their interaction effects.

6.6 Major clinical issues with anxiety disorders and stimulant (including methamphetamine) use

- Anxiety is common amongst stimulant users.
- MAO-Is (either irreversible or reversible) are contraindicated in people using amphetamines or MDMA due to risk of serotonin syndrome. Deaths have been associated with concurrent use of moclobemide and MDMA.
- Individuals should be encouraged to reduce or cease stimulant use so that anxiety symptoms can be better evaluated. In many cases this will result in an overall reduction in anxiety symptoms.
- CBT is also effective in reducing general symptoms of anxiety.
- CBT that focuses on coping mechanisms will be most effective in situations where the individual has been using stimulants to self medicate and cope with social anxiety situations.

**Stimulants
(including
metham-
phetamine)**

6.6.1 Effects of *stimulants* on anxiety disorders

- Anxiety is common amongst stimulant users^(11, 29, 43, 50, 53, 54, 56).
- Anxiety also presents during withdrawal from stimulants⁽⁴⁶⁾.
- The incidence of anxiety increases following stimulant use⁽⁵³⁾.
- Anxiety and its severity is significantly associated with the extent of stimulant use, with higher stimulant use predicting greater severity of anxiety^(50, 53, 55, 56).
- Individuals with childhood anxiety may have increased tendency to use stimulants, in particular ecstasy⁽⁵⁵⁾.

6.6.2 Interactions between *stimulants* and therapeutic agents for anxiety disorders

- MAO-Is (either irreversible or reversible) are contraindicated in people using amphetamines or MDMA due to risk of serotonin syndrome (Appendix 1). Deaths have been associated with concurrent use of moclobemide and MDMA **✖✖✖**^(181, 182).
- Stimulant drugs are likely to exacerbate the effects of SSRI and SNRI antidepressants (and visa versa) and may result in serotonin syndrome (Appendix 1) **✖**^(127, 179, 180). Patients should be warned of signs of serotonin syndrome and be monitored.
- Fluoxetine, norfluoxetine, paroxetine and sertraline are potential inhibitors of CYP 2D6 which metabolises MDMA and methamphetamine. This may result in elevated plasma concentrations leading to toxicity[✖].

6.6.3 Management approaches to comorbid anxiety disorders and stimulant use

- Due to the anxiety-provoking effect of stimulants and the relationship to heavy use, individuals should be encouraged to reduce or cease stimulant use so that anxiety symptoms can be better evaluated. In many cases this will result in an overall reduction in anxiety symptoms.
- Treatment of acute anxiety associated with stimulant withdrawal can be treated with benzodiazepines. However, use should be minimised as those with substance use disorders are at a greater risk of misusing benzodiazepines⁽¹⁹⁶⁾.
- CBT is also effective in reducing general symptoms of anxiety^{****(196, 202, 203)}.
- CBT that focuses on coping mechanisms will be most effective in situations where the individual has been using stimulants to self medicate and cope with social anxiety situations.
- Citalopram and sertraline have the least CYP mediated drug interactions; however, all SSRIs are potential precipitators of serotonin syndrome in people using stimulants.

6.7 Major clinical issues with anxiety disorders and benzodiazepine use

- Tolerance to the sedative effects of benzodiazepines and dependence develops within a short period of time.
- It would appear that tolerance to the anxiolytic effects of benzodiazepines does not develop.
- Graded exposure is a highly effective component in the treatment of anxiety disorders. Patients taking benzodiazepines are unable to benefit from this approach if taking doses greater than 10mg diazepam equivalence and doses below this level may interfere with the person's ability to habituate.
- Benzodiazepine use should be discouraged and reduced, with cessation being a long-term goal, and alternative management strategies introduced.
- CBT is effective in reducing symptoms of anxiety and will be more effective if there is minimal sedation and anxiolysis due to benzodiazepine use.

6.7.1 Effects of benzodiazepines on anxiety disorders

- Due to their anxiolytic effects, benzodiazepines are one of the most commonly prescribed forms of pharmacotherapy in the treatment of anxiety symptoms^(57, 58). They are not, however, the recommended first-line treatment for anxiety disorders.
- Tolerance to the sedative effects of benzodiazepines and dependence develops within a short period of time.
- It would appear that tolerance to the anxiolytic effects of benzodiazepines does not develop⁽¹⁹⁶⁾.
- If short-acting benzodiazepines are used (e.g. alprazolam, oxazepam, temazepam), rapidly fluctuating drug plasma concentrations may exacerbate the symptoms of the anxiety disorder.
- Patients prescribed benzodiazepines for anxiety disorders may be less responsive to and less willing to accept psychological therapies than those who are not.

6.7.2 Interactions between benzodiazepines and therapeutic agents for anxiety disorders

- There is an increased risk of sedation and overdose with the combination of benzodiazepines and sedative antidepressants such as tricyclics and mirtazepine^x.
- Benzodiazepines and antidepressants are both metabolised by CYP 450 enzymes which may result in the inhibition or induction of either drug group. Therefore, individuals should be monitored closely to ensure they are experiencing the appropriate therapeutic effect^x.
- Fluvoxamine will inhibit the metabolism of alprazolam, midazolam, triazolam and diazepam, causing increased plasma concentrations, sedation and potential toxicity^x.
- Citalopram and sertraline are the least likely SSRIs to have cytochrome mediated drug interactions^x.

6.7.3 Management approaches to comorbid anxiety disorders and benzodiazepine use

- Graded exposure is a highly effective component in the treatment of anxiety disorders. Patients taking benzodiazepines are unable to benefit from this approach if taking doses greater than 10mg diazepam equivalence and doses below this level may interfere with the person's ability to habituate to anxiety triggers.
- Benzodiazepine use should be discouraged and reduced, with cessation being a long-term goal and alternative management strategies introduced.
- If large quantities of benzodiazepines (e.g. 40mg diazepam daily equivalent or more) are being consumed then inpatient withdrawal to lower levels should be considered to avoid and manage seizure risk⁽¹⁹⁴⁾.
- If dependence has developed then graduated withdrawal through slow reduction of dosage should be commenced^{****(194-196)}, possibly after transferring the patient onto a long acting benzodiazepine.
- Lower levels of baseline anxiety at the time of benzodiazepine withdrawal are the best predictor of successful taper⁽¹⁹⁶⁾.
- If long-term benzodiazepine use is indicated, then:
 - This should be subject to a contract with the patient.
 - Authorities should be advised, including registration with the relevant local government health authority.
 - The seeking of additional benzodiazepines from other prescribers should be monitored (e.g. using the *Authority to release personal PBS claims information to a third party form*).
 - Daily or weekly dispensing of benzodiazepines should be considered and may assist with controlling use.
- CBT is effective in reducing symptoms of anxiety^{****(202)} and will be more effective if there is minimal sedation and anxiolysis due to benzodiazepine use⁽¹⁹⁶⁾.
- CBT has been shown to improve the likelihood of patients successfully tapering and ceasing benzodiazepines when they also have an anxiety disorder^{***(203, 204)}.

- Antidepressant medication (SSRIs or other non-sedating antidepressants) can be commenced with the patient still taking benzodiazepines.
- Citalopram and sertraline are the least likely SSRIs to have cytochrome mediated drug interactions.

6.8 Major clinical issues with anxiety disorders and **inhalant/solvent use**

- Inhalant users have higher rates of anxiety disorders.
- The sedative effects of antidepressants and benzodiazepines may be exacerbated by inhalants and may possibly result in severe sedation and overdose.
- As with most other substances, inhalant users should be encouraged to reduce or cease use to observe whether anxiety symptoms resolve.

6.8.1 *Effects of **inhalants/solvents** on anxiety disorders*

- Inhalant users have higher rates of anxiety disorders. Causal relationships are unclear^(249, 250).

6.8.2 *Interactions between **inhalants/solvents** and therapeutic agents for anxiety disorders*

- The sedative effects of antidepressants and benzodiazepines may be exacerbated by inhalants and may possibly result in severe sedation and overdose^x.
- Most antidepressants lower seizure threshold and tricyclic antidepressants can cause cardiac arrhythmias. Therefore, risks should be appraised prior to commencement^x.

6.8.3 *Management approaches to comorbid anxiety disorders and **inhalant/solvent use***

- There is no literature that sheds light on managing people with both anxiety and inhalant/solvent use related problems.
- As with most other substances, inhalant users should be encouraged to reduce or cease use to observe whether anxiety symptoms resolve.
- In general with respect to inhalant/solvent use⁽⁶⁵⁾:
 - Outline the harms associated with inhalant/solvent use.
 - Investigate polysubstance use as this is common.
- Standard CBT approaches to both sets of issues should be used, with particular attention to the development of:
 - Assertiveness skills (refusal skills).
 - Coping skills for controlling and managing emotions such as anger and sadness.

Offer alternatives to inhalant use, for example, recreational activities.

- Community reinforcement approaches should be developed by mobilising the local health and welfare service system in individual care plans.
- Family interventions need to be considered, for example, increasing communication between the person and the family.
- Assertive outreach and follow-up may be required.