

11 Gambling and substance use

11.1 Gambling

Problem gambling affects a large proportion of the population⁽⁴²⁶⁻⁴²⁹⁾. Pathological gambling is listed in the DSM-IV as an impulse control disorder. These disorders are initially driven by pleasure, arousal and gratification.

Recurrent gambling behaviour causes significant disruptions in personal, family, social and vocational pursuits⁽⁴²⁶⁻⁴²⁹⁾. People preoccupied with gambling may report that they are seeking action or an aroused, euphoric state, more so than the money itself^(426, 428).

The features of pathological gambling are persistent. Over time, patients develop unpleasant feelings, physiological activation and dysphoria which are relieved when the compulsive behaviour is undertaken.

In a manner similar to substance use disorders, as the opportunities for gambling increase (e.g. easily accessible internet gambling can be likened to an increase in the 'supply' of a substance of misuse), so does the proportion of the population that develops gambling associated problems. Hence, gambling disorders and problem gambling continue to rise^(426, 428-430).

Gambling addictions typically begin in early adolescence in males and later in life for females^(428, 431). Males are significantly more likely to experience gambling-related problems than females⁽⁴³¹⁻⁴³⁶⁾.

Gambling is a complex phenomenon and may also be viewed as:

- An addiction:
 - Tolerance can develop as people feel the need to spend increasing amounts of time and money in order to achieve the same level of excitement^(426, 428).
 - Withdrawal symptoms can occur on cessation of gambling and can resolve on recommencement of gambling^(426, 428).
 - Self medication theories of other mental disorders are also applied to gambling as they can be to chemical substances of addiction^(426, 428).

There is evidence, however, that gambling behaviours persist over time in contrast to substance use related problems which become less prevalent as people age^(68, 432, 437).

- An affective disorder.
- A specific type of obsessive compulsive disorder.

The above theories have provided the theoretical rationale for the use of certain pharmacological agents to treat people affected by problem gambling^(427, 438).

The clinical course of gambling can be separated into three phases⁽⁴²⁸⁾.

- **Winning:** Wins are greatly dramatised and losses are often forgotten about and even denied.
- **Losing:** The individual begins to gamble less cautiously in an attempt to win back lost finances and impending losses mount.

- **Desperation:** Gambling is frequently associated with criminality and legal problems in an attempt to gain more money to gamble^(428, 439, 440). Debts grow, individuals may be prosecuted and guilt and depression set in leading to suicide.

Management approaches

- Treatment of problem gambling is often delayed due to cognitive distortions and denial⁽⁴²⁸⁾.
- Few clinicians are skilled in the area of treatment of problem gambling⁽⁴³⁰⁾.
- CBT, in particular, exposure therapy is effective at reducing problem gambling^{****(441-443)}.
- Motivational approaches are also effective when used in the treatment of problem gambling^{***(444)}.
- Pharmacological treatments for gambling are more effective than no treatment or placebo^{****(445)}.
- There are three broad classes of pharmacological agents used in an attempt to treat and manage problem gambling. These are antidepressants, opioid antagonists and mood stabilisers^(438, 445, 446).
- There appears to be no significant difference in outcome between the three main classes of pharmacological interventions used^{****}. However, it may be that some people with problem gambling with specific comorbidities may benefit more from certain drug interventions than others⁽⁴⁴⁵⁾.

Antidepressants

SSRIs

- SSRIs have been used when problem gambling is viewed as an OCD or an affective disorder^{r(427)}.
- If there is any benefit, doses of SSRIs used in the treatment of gambling may need to be higher and require administration for longer periods of time before a response is observed^(428, 447).
- The effect of SSRIs appear to be independent of underlying depressive symptoms^{****(447-450)}.
- Fluvoxamine^{***(448, 451)} and citalopram^{*(450)} have been shown to significantly improve overall gambling severity [reduced urge to gamble, reduced number of days gambled, reduced amount of money lost]. Results for paroxetine are mixed^(449, 452).
- SSRIs are well tolerated when used for these indications^{c(448, 453)}.

Other antidepressants

- Bupropion is also effective in reducing gambling scale scores as well as global functioning scale scores and is as effective as naltrexone in producing full responders to gambling treatment^{****(454)}.
- Note: Bupropion is not currently indicated for problem gambling in Australia.

Opioid antagonists

The mechanism by which naltrexone may be effective in reducing problem gambling is by reducing the urge to gamble^{****(454-456)}.

Mood stabilisers and anticonvulsants

- A study of small numbers of people using mood stabilisers for the treatment of gambling alone (valproate and lithium) has shown promise in reducing gambling. However, few conclusions are able to be drawn from this single study^{***(457)}.
- Topiramate is as effective in reducing gambling as fluvoxamine with even more individuals in full remission following topiramate than fluoxetine, as well as higher treatment compliance following topiramate^{***(458)}.
- Note: Topiramate is not currently indicated for problem gambling in Australia.

11.2 Comorbidity with gambling

11.2.1 Gambling and substance use

- There is a high prevalence of current and lifetime substance use amongst people who are affected by problem gambling, exceeding that of the general population^(426, 428, 431, 432, 435-437, 443, 459-462).
- There is also a strong correlation between the severity of substance use and the severity of problem gambling, with higher rates and severity of substance use being predictive of more severe gambling problems and vice versa^(23, 365, 367, 428, 429, 433, 463).
- Substance use can be a significant discriminator between people with problematic versus non-problematic gambling. The greater the number of substances used the more severe the gambling problems experienced^(367, 463, 464).
- Problem gambling is often associated with increased impulsivity, antisocial tendencies as well as the inability to control anger^(426, 465-468).
- Gambling at an earlier age increases the risk of multiple addictions and risky behaviour⁽⁴³⁷⁾.
- People with comorbid substance use and gambling problems experience increased impulsivity which leads to further poor decision making⁽⁴²⁸⁾.
- Impaired impulse control and poor risk assessment occurs with both gambling and substance use disorders^(365, 428).
- Failure to treat comorbid substance use disorders in gambling may lead to higher gambling relapse rates⁽⁴²⁸⁾.
- People with comorbid substance use and gambling problems are more likely to report other psychiatric histories⁽⁴³³⁾.

11.2.2 *Gambling and mental disorders*

- Increased gambling is associated with reduced mental health status⁽⁴⁶⁹⁾. The majority of people with problem gambling have more than one psychiatric disorder⁽⁴⁵⁹⁾.
- The causative relationship between comorbid problem gambling and other mental disorders has not been clearly established:
 - Gambling may be pursued to relieve anxiety⁽⁴²⁸⁾ and depression⁽⁴²⁹⁾.
 - Early onset problematic gambling is associated with pre-existing depression⁽⁴⁷⁰⁾.
 - Mental disorders such as depression and anxiety may develop or be exacerbated by gambling⁽⁴²⁸⁾.
 - People most at risk for problem gambling are those with major mental disorders who often experience significant social isolation and separation⁽⁴²⁹⁾.
 - Use of psychiatric medication has shown a decline following behavioural and motivational treatment of problem gambling⁽⁴⁶⁴⁾. This suggests that anxiety and depression may be secondary to gambling, at least in some people.
- Women are more likely than men to have additional mood or anxiety disorders and use gambling to escape depressed moods^(428, 431, 471). Women with problem gambling are also significantly more likely to seek treatment for their mood or anxiety disorder⁽⁴³¹⁾.
- Affective disorders are more common amongst people who are affected by problem gambling compared to the general population^(428, 429, 432, 434, 437, 440, 459, 462, 465, 466, 469, 471-478).
- Gambling is more common amongst people with bipolar disorder than the general population^(462, 479).
- Higher rates of anxiety are also correlated with more severe gambling problems^(23, 480).
- There are also increased rates of obsessive compulsive disorders in people with problem gambling^(427, 428, 438, 459, 460, 481).
- As mentioned above, problem gambling is also highly correlated with personality disorders, particularly antisocial, borderline and obsessive compulsive personality disorders^(428, 435, 437, 465, 470, 471, 482, 483).
- Problem gambling is associated with high comorbidity of other impulse control disorders (including kleptomania, impulsive shopping and impulsive sexual behaviour), as well as purging type eating disorders^(364-367, 432, 462, 484).

11.2.3 *Gambling and suicide*

- Problem gambling is often associated with increased suicidal ideation and attempts compared to the general population^(427-429, 432, 437, 472, 476, 477, 485).
- Early onset problem gambling increases lifetime risk of suicide⁽⁴⁷⁰⁾.
- However, gambling-related suicide attempts are usually made by older people with problem gambling⁽⁴⁸⁵⁾.
- Both comorbid substance use^(432, 433) and comorbid mental disorders increase the risk of suicide in people with problem gambling⁽⁴⁸⁵⁾.

11.2.4 **General management approaches to comorbidity**

- A history of past substance use and mental disorders does not lessen the effectiveness of current treatment for gambling⁽⁴⁶⁴⁾.
- People with current substance use as well as problem gambling must avoid replacing one addiction with the other⁽⁴³⁶⁾.
- People with problem gambling and bipolar spectrum disorder show significant improvement on gambling thoughts, urges and behaviour as well as in manic behaviour while taking lithium ^{***}(486).
- SSRIs as a combined treatment may be effective in treating co-occurring anxiety and gambling ^{*}(487) as well as depression.

11.3 Major clinical issues with gambling and **cannabis/hallucinogen use**

- There is a significant association between cannabis use and problem gambling, with more severe problem gambling being associated with greater intensity of cannabis use and vice versa.
- CBT approaches that target both gambling and cannabis use may be effective in people with comorbid cannabis use disorders and problem gambling.

11.3.1 **Effects of cannabis and other hallucinogens on problem gambling**

- As is the case with the general population, cannabis is the most commonly used illicit substance amongst people with problem gambling^(432, 464, 488).
- There is a significant association between cannabis use and problem gambling with more severe problem gambling being associated with greater intensity of cannabis use and vice versa^(365, 436, 440, 443, 464, 468, 470).
- Additional hallucinogen use is also reported by people with problem gambling although not to the same extent as cannabis^(432, 464).

11.3.2 **Interactions between cannabis and other hallucinogens and therapeutic agents for problem gambling**

- Cannabis can exacerbate the sedative effects of tricyclic antidepressants and mood stabilisers (lithium and sodium valproate). This 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 ensure responses are within the therapeutic range[✗].

11.3.3 Management approaches to comorbid problem gambling and cannabis use

- 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, in particular, exposure therapy is effective at reducing problem gambling^{****(441-443)}.
- CBT approaches that target both gambling and cannabis use may be effective in people with comorbid cannabis use disorders and problem gambling. However, studies are yet to confirm this.

11.4 Major clinical issues with gambling and alcohol use

- Problem gambling and alcohol use frequently co-occur.
- Comorbid gambling and alcohol use increase the risk of suicide.
- Alcohol can exacerbate the sedative effects of tricyclic antidepressants and mood stabilisers (lithium and sodium valproate).
- Alcohol consumption will interfere with the effectiveness of exposure based treatments for gambling.
- As naltrexone has been shown to improve problem gambling, it may be an effective treatment to manage both problem gambling and alcohol consumption.
- CBT that addresses both gambling behaviour and alcohol use may also be an effective treatment for comorbid problem gambling and alcohol consumption.

11.4.1 Effects of alcohol on problem gambling

- Problem gambling and alcohol use frequently co-occur, with alcohol use being the most common substance used in people with problem gambling^(432, 433, 435, 460, 462, 464, 468, 478, 483, 488, 489).
- Increased severity of problem gambling is associated with heavy drinking^(23, 365, 431, 434, 440, 466, 467, 469, 470, 490).
- Alcohol consumption results in increased rates of play in gambling and prolongs gambling episodes^(491, 492).
- Comorbid gambling and alcohol use increase the risk of suicide⁽⁴⁹³⁾.

11.4.2 Interactions between alcohol and therapeutic agents for problem gambling

- Alcohol can exacerbate the sedative effects of tricyclic antidepressants and mood stabilisers (lithium and sodium valproate). This increases the risk of impaired driving and injury as well as overdose[✗].
- Alcohol can exacerbate the sedative effects of some antidepressants including tricyclic antidepressants and mirtazepine. Alcohol toxicity and risk of overdose may occur through the inhibition of CYPs by sedative antidepressants involved in the metabolism of alcohol^{✗(133)}.
- Interactions between antidepressants and acamprosate used to treat alcohol dependence are minimal as are interactions between antidepressants and disulfiram and naltrexone also used to treat alcohol dependence⁽¹³⁴⁾.

11.4.3 Management approaches to comorbid problem gambling and alcohol use

- Alcohol consumption will interfere with the effectiveness of exposure based treatments for gambling.
- If large quantities of alcohol are being consumed, then inpatient withdrawal or detoxification 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⁾.
- Acamprosate and naltrexone are both effective in the management of alcohol dependence and maintaining abstinence ****(141, 144, 235, 236).
- As naltrexone has been shown to improve problem gambling ****(454-456), it may be an effective treatment to manage both problem gambling and alcohol consumption ****(235, 236, 494). However, large scale trials are yet to confirm this.
- SSRIs may be effective in managing problem gambling ***(448, 450, 451), particularly in those people with comorbid alcohol use and depression ***(130, 135-137). However, large scale trials are yet to confirm this.
- CBT, in particular exposure therapy, is effective at reducing problem gambling ****(441-443).
- CBT that addresses both gambling behaviour and alcohol use may also be an effective treatment for comorbid problem gambling and alcohol consumption.

11.5 Major clinical issues with gambling and opioid use

- Heroin use is relatively rare among people with problem gambling. The use of prescription opioids is more common.
- However, problem gambling is prevalent among people on methadone maintenance.
- Buprenorphine impairs decision-making less than methadone maintenance in opioid dependent individuals and may therefore be more beneficial when used to manage people with opioid dependence and problem gambling.

11.5.1 Effects of opioids on problem gambling

- Heroin use is relatively rare among people with problem gambling⁽⁴⁶⁴⁾. The use of prescription opioids is more common^(432, 464).
- However, amongst people on methadone maintenance:
 - Problem gambling is prevalent^(495, 496).
 - People with problem gambling are more likely to use other substances when compared with people whose gambling is non-problematic⁽⁴⁹⁵⁾.
 - Problem gambling negatively impacts program retention rates⁽⁴⁹⁵⁾.
 - People with problem gambling report poorer mental health status than people whose gambling is not problematic⁽⁴⁹⁶⁾.

11.5.2 Interactions between **opioids** and therapeutic agents for problem gambling

- Opioids can exacerbate the sedative effects of tricyclic antidepressants and mood stabilisers (lithium and sodium valproate). This increases the risk of impaired driving and injury as well as overdose^x.
- Fluvoxamine^{xxx}, fluoxetine^{xx}, norfluoxetine^{xx} 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^{xxx(151-155)}.
- Fluvoxamine is the most potent inhibitor of methadone and buprenorphine metabolism and is the most clinically relevant, therefore, it should be avoided^{xxx(150)}.
- Fluoxetine and paroxetine should also be avoided^{xx}.
- 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)}.

Opioids

11.5.3 Management approaches to comorbid problem gambling and **opioid** use

- As naltrexone has been shown to improve problem gambling^{****(454-456)} and be effective in the management of opioid dependence^{***(497)}, it may be useful in the treatment of comorbid problem gambling and opioid dependence. However, there have been no studies to confirm this and compliance is likely to be an issue.
- Buprenorphine improves decision making compared to methadone maintenance in opioid dependent individuals^{***(498)} and may therefore be more beneficial when used to manage people with opioid dependence and problem gambling.

11.6 Major clinical issues with gambling and stimulant (including methamphetamine) use

- Stimulant users are frequently affected by problem gambling.
- MAO-Is (either irreversible or reversible) are contraindicated in people using amphetamines or MDMA. Deaths have been associated with concurrent use of moclobemide and MDMA.

11.6.1 Effects of stimulants on problem gambling

- Rates of stimulant use are higher in people with problem gambling than the general population⁽⁴⁸⁸⁾. Stimulant users are frequently affected by problem gambling⁽⁴³⁹⁾.
- Stimulants may increase risk taking and impulsivity^(338, 339) and are therefore likely to adversely affect people with problem gambling.
- Stimulants are amongst the most commonly used illicit substances by people with problem gambling^(432, 464).

11.6.2 Interactions between stimulants and therapeutic agents for problem gambling

- Stimulant drugs are likely to exacerbate the effects of SSRI and SNRI antidepressants, in particular (and vice versa), and may result in serotonin syndrome (Appendix 1)✕^(127, 179, 180). Patients should be warned of signs of serotonin syndrome and be monitored.
- MAO-Is (either irreversible or reversible) are contraindicated in people using amphetamines or MDMA. Deaths have been associated with concurrent use of moclobemide and MDMA✕✕✕^(181, 182).
- 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✕.

11.6.3 Management approaches to comorbid problem gambling and stimulants use

- Formal drug detoxification should be considered if the person is dependent on stimulants.
- CBT is effective in reducing stimulant use^{***^(49, 183)} as well as problem gambling^{****⁽⁴⁴¹⁻⁴⁴³⁾} and an approach that integrates treatments for both conditions may be more effective in managing comorbid stimulant use and problem gambling. This is yet to be investigated.

11.7 Major clinical issues with gambling and benzodiazepine use

- Benzodiazepines will interfere with response to psychological treatments in a dose-related manner.
- Benzodiazepine use should be discouraged and reduced. Cessation should be a long-term goal with the introduction of alternative management strategies.

11.7.1 Effects of benzodiazepines on problem gambling

- Comorbid benzodiazepine use and gambling is not commonly reported.
- High doses of benzodiazepines (or low doses combined with alcohol) can increase risk taking, impulsive behaviours⁽⁴⁹⁹⁾ and cognitive impairment, all of which are likely to result in adverse consequences in people with problem gambling.

11.7.2 Interactions between benzodiazepines and therapeutic agents for problem gambling

- Benzodiazepines can exacerbate the sedative effects of tricyclic antidepressants, and mood stabilisers (lithium and sodium valproate). This increases the risk of impaired driving and injury as well as overdose✘.
- 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✘.
- Fluvoxamine will inhibit the metabolism of alprazolam, midazolam, triazolam and diazepam causing increased sedation and potential toxicity✘.
- Citalopram and sertraline are the least likely SSRIs to have cytochrome mediated drug interactions✘.

11.7.3 Management approaches to comorbid problem gambling and benzodiazepine use

- Benzodiazepines will interfere with response to psychological treatments in a dose-related manner⁽¹⁹⁶⁾.
- Benzodiazepine use should be discouraged and reduced. Cessation should be a long-term goal with the introduction of alternative management strategies.
- 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.

Stimulants
(including
metham-
phetamine)

Benzo-
diazepines

- 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.

11.8 Major clinical issues with gambling and **inhalant/solvent** use

11.8.1 *Effects of **solvents/inhalants** on problem gambling*

Inhalant use is relatively rare among people with problem gambling⁽⁴⁶⁴⁾ and appears to be one of the least misused classes of substances reported by people with problem gambling^(432, 485).

11.8.2 *Interactions between **solvents/inhalants** and therapeutic agents for problem gambling*

- Inhalants can exacerbate the sedative effects of tricyclic antidepressants, and mood stabilisers (lithium and sodium valproate). This increases the risk of impaired driving and injury as well as overdose[✗].
- Most antidepressants reduce seizure threshold. Therefore, risks should be appraised prior to commencement[✗].

11.8.3 *Management approaches to comorbid problem gambling and **inhalant/solvent** use*

- As with most other substances, inhalant users should be encouraged to try and reduce or cease use.
- 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.