Depression

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Clinical presentation

Depressive symptoms include low mood; markedly diminished interest or pleasure in all, or most activities; sleep disturbances; appetite disturbances; irritability; fatigue; psychomotor agitation or retardation; poor concentration; feelings of guilt, hopelessness, helplessness and worthlessness; and suicidal thoughts (refer to Chapter A4).

Managing depressive symptoms

Negative mood is often a trigger for relapse, and therefore addressing depressive symptoms is also an important part of relapse prevention [557]. The techniques outlined in Table 37 may help AOD workers to manage clients with depressive symptoms.

A number of simple strategies based on CBT are also useful in managing clients with these symptoms, including [310, 386]:

- Cognitive restructuring.
- Pleasure and mastery events scheduling.
- Goal setting.
- Problem solving.

These techniques are discussed in greater detail in Appendix T.

It is important to note that many depressive symptoms (and many anxiety symptoms) will subside after a period of abstinence and stabilisation [35, 290, 299]. It is useful to explain to clients that it is quite normal to feel depressed (or anxious) when entering treatment but that these feelings usually improve over a period of weeks. During and after this time, constant monitoring of symptoms will allow the worker to determine if the client requires further treatment for these symptoms. If the client has a history of depressive episodes in circumstances when he/she is not intoxicated or withdrawing, he/she may have an independent depressive disorder. For these clients, it is unlikely that their depressive symptoms will resolve completely with abstinence – indeed their symptoms may even increase. In such cases, clients should be assessed for a depressive disorder and the treatment options described in this chapter should be considered.

Table 37: Dos and don'ts of managing a client with depressive symptoms of bipolar

Do:

- ✓ Encourage and emphasise successes and positive steps (even just coming in for treatment).
- ✓ Take everything they say seriously.
- ✓ Maintain eye contact and sit in a relaxed position – positive body language will help you and the client feel more comfortable.
- ✓ Use open-ended questions such as 'So tell me about...?' which require more than a 'yes' or 'no' answer. This is often a good way to start a conversation.
- ✓ Constantly monitor suicidal thoughts and talk about these thoughts openly and calmly.
- ✓ Encourage the client to express his/her feelings.
- ✓ Be available, supportive and empathetic.
- ✓ Offer realistic hope (i.e., that treatment is available and effective).
- ✓ Provide contact details of counselling services and offer to make referrals if required (many depressed people struggle to do this alone).
- ✓ Encourage participation in healthy, pleasurable and achievement-based activities (e.g., exercise, hobbies, work).

Don't:

- × Make unrealistic statements or give unrealistic hope, like 'everything will be fine'.
- × Invalidate the client's feelings.
- × Be harsh, angry, or judgemental. Remain calm and patient.
- × Act shocked by what the client may reveal.

Adapted from Scott et al. [558] and Clancy and Terry [296].

Treating depressive disorders

There are several treatment options available for the treatment of depressive disorders, including psychotherapy, pharmacotherapy,ECT, e-health, physical activity, as well as complementary and alternative therapies (e.g., omega-3). The evidence base surrounding each of these treatments is discussed below.

Psychotherapy

Research on psychological therapies provides support for the use of integrated psychological treatments for comorbid depression and AOD use disorders [165, 600]. However, the small number of studies, variation in study results, and small sample sizes used in these studies highlight the need for larger trials to be conducted in this area [601].

The majority of studies to date have examined the use of integrated treatments that adopt a CBT approach [272, 386, 432, 602, 603]. In a review of the literature, Hides and colleagues [601] note that CBT appears to yield superior results for symptoms of depression and AOD use when compared to no treatment, but there is little evidence demonstrating that CBT is more effective when compared with other forms of psychological therapy (e.g., relaxation training, MI, integrated MI/CBT). As a way of enhancing CBT, it has been suggested that CBT be combined with other evidence-based psychological approaches, such as contingency management (see Chapter B5). The combination of CBT plus contingency management has been found to be more effective than either CBT or contingency management alone in the treatment of this comorbidity [418, 604, 605].

Baker and colleagues [386] examined the effectiveness of a brief CBT intervention targeting amphetamine use, and found that a reduction in depressive symptoms accompanied a reduction in amphetamine use, suggesting that interventions designed to reduce AOD use may have promising outcomes for symptoms of depression.

Another approach showing promise in the treatment of comorbid AOD use and depression is behavioural activation. Originally developed in the 1970s, behavioural activation is based entirely on behavioural strategies [606]. The therapy is based on the notion that problems in the lives of vulnerable people reduce their ability to experience positive reward from their environments, leading to symptoms and behaviours characteristic of depression. Behavioural activation aims to activate clients in specific ways that will increase rewarding experiences in their lives. It also focuses on processes that reduce activation, such as escape and avoidance behaviours including AOD use.

There is empirical evidence to suggest that behavioural activation is just as effective in treating depression as combined cognitive and behavioural techniques and antidepressant medication [607, 608]. Behavioural activation has the added benefit of being more time efficient and less complex than most other psychotherapies, and can therefore be delivered by less experienced therapists [608]. Another advantage of behavioural activation is that it incorporates some essential components of AOD treatment, such as social support, emotional expression, reordering of life priorities, stress management, avoidance reduction, symptom control and health education [609].

To date, three small RCTs have found support for the use of behavioural activation among people with AOD use disorders. The first examined the efficacy of adding behavioural activation for depression to standard inpatient AOD treatment among a small sample of illicit drug users with depressive symptoms [610]. The authors found that patients who were randomised to receive behavioural activation demonstrated significantly greater improvements in depression at post-treatment compared with standard care alone. They also reported significantly higher treatment satisfaction scores. The same treatment was subsequently compared with an attention control condition among people in residential AOD treatment, and was found to be superior in terms of treatment retention and levels of activation [611]. A third trial examined the efficacy of behavioural activation paired with standard smoking cessation strategies (including NRT) compared with standard smoking cessation strategies alone (including NRT) [612]. Participants randomised to receive behavioural activation demonstrated greater reductions in depressive symptoms and a higher rate of smoking abstinence than did those randomised to receive standard smoking cessation strategies. Collectively, these pilot studies provide promising support for the use of behavioural activation among individuals with comorbid depression and AOD use, however, further trials are needed. A large RCT comparing the efficacy of behavioural activation added to standard AOD treatment with standard AOD treatment alone is currently underway in Australia.

Lastly, although still in the early stages, there is preliminary support for mindfulness-based relapse prevention in the treatment of co-occurring depression and AOD use [613].

Pharmacotherapy

There is consensus amongst experts that pharmacotherapy (i.e., antidepressants; see Table 38) for comorbid depression and alcohol use disorders is effective, provided an individualised approach is used [424, 432]. Unless there are significant contraindications, it appears clinically appropriate to use medication that has been proven efficacious in the treatment of major depression in those depressed patients with an AOD use disorder.

Thase and colleagues [424] comment on the sometimes over-restrictive attitudes towards pharmacological treatments for depressive disorders among people with AOD use disorders, where clients can present in a state of physical and emotional despair that requires immediate intervention. Considering the safety of

most of the newer antidepressants such as SSRIs, such caution as waiting for a minimum number of weeks of abstinence cannot be justified. This would particularly apply where a client has a history of depression during periods of abstinence, or where the person has had successful antidepressant intervention in the past. Clients being commenced on antidepressants should nonetheless be carefully monitored as there have been some well-publicised cases of increased suicidality on commencement of antidepressant treatment [614]. Such incidents are rare and there is much conflicting and contradictory evidence on the clear link between antidepressant-induced suicidality [615, 616]. Thus, although it is suggested that the benefits of antidepressant use outweigh the risks, and appropriate use actually protects depressed patients from suicide [617], it is important to maintain appropriate monitoring of suicidality [618].

Reviews have generally found that among clients with comorbid alcohol and depressive disorders, treatment with tricyclic antidepressants (TCAs) and SSRIs has a significant effect on symptoms of depression, but effects on alcohol use have been equivocal [424, 432, 539]. A more recent review found mixed findings regarding depressive symptoms. Antidepressants were generally found to be effective in treating symptoms of depression however, when the effectiveness of SSRIs were examined separately, there were no significant treatment effects on depressive symptoms, relative to placebo [619]. Ioveno and colleagues [619] speculated that this may be due to high placebo response rates in these trials, and therefore further studies examining the use of SSRIs in this comorbid group are required.

Alcohol use responds well where depressive symptoms have been reduced, but sustained abstinence is not usually achieved [620-623]. There have been some studies which have shown a relatively negative effect on alcohol consumption in alcohol-dependent young men prescribed SSRIs [624-627]. Antidepressants that do not come under the umbrella of SSRIs or TCAs have been found to be effective in single studies [628, 629].

Compared to the newer antidepressants, TCAs are poorly tolerated, potentially lethal in overdose, and cause significant adverse effects when combined with other central nervous system depressants. In contrast, SSRIs are associated with fewer side effects, have better tolerability (resulting in improved compliance) and are safer in overdose [121, 424]. Despite their efficacy, some clients may be reluctant to take SSRIs due to the misconception that they are 'addictive'. SSRIs are not habit-forming; however, users may experience a discontinuation syndrome if the medication is stopped abruptly [121]. Symptoms are similar to some of those experienced during alcohol or opiate withdrawal (e.g., flu-like symptoms, light-headedness, headache, nausea) [121]. When discontinuing SSRIs, the dose should be gradually tapered.

Although studies of comorbid alcohol dependence and major depression support the use of SSRIs, studies of cocaine and opiate dependent clients do not [263]. At present, there is limited evidence to support the use of antidepressants in treating depressed opioid dependent persons currently receiving opioid agonist treatment. In a recent systematic review, Pani and colleagues [631] noted that the evidence in this area was highly limited due to the small number of studies conducted, and methodological limitations within these studies. Whilst there was some evidence of a trend towards improved outcomes for depression symptoms and AOD use for clients receiving antidepressants as well as opioid agonists, there were no statistically significant differences in outcomes between antidepressant and placebo groups.

Table 38: Antidepressant medications

Drug type and name	Brand names
Tricyclic antidepressant (TCA):	
Amitriptyline	Endep
Dothiepin	Dothep, Prothiaden
Nortriptyline	Allegron
Doxepin	Deptran, Sinequan
Imipramine	Tofranil, Tolerade
Clomipramine	Anafranil, Placil
Trimipramine	Surmontil
Monoamine oxidase inhibitor (MAOI):	
Tranylcypromine	Parnate
Phenelzine	Nardil
Reversible inhibitor of monoamine oxidase A (RIMA):	
Moclobemide	Aurorix, Clobemix, Amira
Selective serotonin reuptake inhibitor (SSRI):	
Fluoxetine	Lovan, Prozac, Zactin
Paroxetine	Aropax, Paxtine, Paroxo
Sertraline	Zoloft, Eleva, Seralin
Fluvoxamine	Luvox, Faverin, Voxam
Citalopram	Cipramil, Celapram, Celica
Escitalopram	Lexapro, Escicor, Esipram
Serotonin and noradrenaline reuptake inhibitor (SNRI):	
Venlafaxine	Efexor-XR
Desvenlafaxine	Pristiq
Duloxetine	Cymbalta
Noradrenaline and specific serotonergic agent (NaSSA):	
Mirtazapine	Avanza, Axit, Mirtazon
Tetracyclic antidepressant:	
Mianserin	Tolvon, Lumin
Noradrenaline reuptake inhibitor (NRI):	
Reboxetine	Edronax
Melatonergic antidepressant:	
Agomelatine	Valdoxan

Adapted from Australian Government Department of Health [630]. For a full list of generic brands available, see the Therapeutic Goods Administration website (https://www.tga.gov.au/).

Different types of antidepressants seem to be suitable for different types of substance use disorders [416]. In particular, individuals with AOD use disorders tend to respond better to antidepressants that have a similar direct or side effect profile to their substance of abuse. Hence, the more sedating antidepressants such as doxepin or paroxetine are more effective in depressed abusers of alcohol, heroin and sedatives, and the more stimulating antidepressants such as desipramine and bupropion have greater efficacy in depressed abusers of stimulants and nicotine. As there are no guidelines as yet for the treatment of comorbidity with depression in users of psychostimulants such as amphetamines and ecstasy [632], the use of the more stimulating antidepressants for these clients provides the best guidance at this time.

For all AOD clients, extreme caution should be taken when prescribing monoamine oxidase inhibitors (MAOIs). These medications are potentially dangerous because of the dietary and medication restrictions involved [121]. Hypertensive crisis with intracranial bleeding and death can occur if combined with a tyramine-rich diet or contraindicated medications (including opioid and psychostimulant substances, such as over-the-counter cold and flu medications) [121, 263]. For this reason, MAOIs should only be used when other medication options have failed.

It is important to note that it can take up to four weeks for an antidepressant to reach therapeutic levels in the blood. Responses to antidepressants are typically noticeable within two to four weeks, with continued improvement in symptoms for up to 12 weeks [633-635]. If little or no improvement in mood occurs over the induction time specified by the drug manufacturer and the medication is being taken as prescribed, consideration should be given to increasing the dose within the recommended range. If still little or no improvement is observed, switching or augmenting with another antidepressant may be considered. It is recommended that there be at least one within-class switch before considering augmentation or other options, keeping in mind the potential for drug interactions, and the adverse effects of some antidepressants [633-636].

Two medications that have been used for treating alcohol use disorders – naltrexone and acamprosate – have shown moderately positive outcomes in this single disorder [637-641]. Disulfiram can also be an effective treatment for some people with alcohol problems, particularly those who are highly motivated and who can be closely supervised. Research suggests that naltrexone, acamprosate, and disulfiram are all tolerated well in clients with comorbid depression [642].

Naltrexone has been found to be associated with better drinking outcomes in clients being treated with antidepressants for their depression and anxiety [643]. With little support for the use of antidepressants alone to reduce excessive drinking, more recent research indicates that the use of antidepressants combined with naltrexone may lead to improved outcomes. Pettinati and colleagues found that when sertraline and naltrexone were combined in the treatment of co-occurring depression and alcohol dependence, there were better outcomes in terms of abstinence and relapse, relative to either sertraline or naltrexone alone, or placebo [644].

It should also be borne in mind that at least for naltrexone, treatment beyond 12 weeks may not improve drinking outcomes in those with alcohol use disorders alone [645]. While both acamprosate and naltrexone are available on the Pharmaceutical Benefits Scheme for alcohol dependence, disulfiram is expensive and only available with a private prescription. Although only a tentative finding requiring further research, another study found that buprenorphine had better outcomes with opiate abusers with comorbid depression than those who were not depressed [646]. This suggests that buprenorphine may prove to be an especially useful pharmacotherapy for this sub-group.

Electroconvulsive therapy (ECT)

ECT can be an effective treatment for certain patients. There is evidence that ECT is an effective treatment for depression as a single disorder [647]; however, no research studies to date have assessed the efficacy of ECT in treating co-occurring depression and AOD use disorders. The Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for the treatment of depression note that ECT is a highly efficacious treatment with a strong evidence base, particularly for severe depressive disorders [648, 649]. The UK NICE Guidelines similarly recommend that ECT be considered for treating severe depressive disorders, or after other treatment options have been exhausted [650].

E-health interventions

Research examining e-health interventions for depression based on CBT therapies has found evidence of successful outcomes [449], and their use as the optimal low-intensity treatment for adults experiencing depression has been recommended by the UK NICE Guidelines [444]. Recommended programs include *Beating the Blues* and *MoodGYM* both of which have been found to improve a range of depression outcomes [651-653]. Neither of these programs, however, address comorbid AOD use.

A small number of e-health interventions specifically designed to treat comorbid depression and AOD use have been evaluated. The *SHADE* program, consisting of nine sessions of interactive exercises based on MI and CBT, has been associated with moderate to large effect sizes for alcohol consumption and significant reductions in depression scores over 12-month follow-up [654, 655]. More recently, a brief (4-session) early intervention program called the *DEAL Project* was developed, targeting young people experiencing depression with harmful patterns of alcohol use [656]. The program is undertaken entirely online with no clinician support. In evaluating the intervention, Deady and colleagues [657] found that individuals randomised to receive the *DEAL Project* demonstrated a greater reduction in symptoms of depression and alcohol use compared to individuals randomised to an attention-control condition.

One other study has examined the use of a single-session of online personalised feedback and psychoeducation provided to college students [658]. The study compared alcohol feedback only, depressed mood feedback only, integrated feedback, and an assessment only condition. At 1-month follow-up, no differences in depressed mood or alcohol use were found across the conditions.

Physical activity

There is increasing evidence to suggest that regular physical exercise has psychological benefits, with more active people illustrating lower levels of depression than sedentary people [659-661]. As mentioned previously, exercise is relatively low-risk, is associated with wide physical health benefits, and research has demonstrated exercise to be as effective in reducing depressive symptoms as psychotherapy and antidepressants [185, 195, 662]. A Cochrane review concluded that physical activity (defined as aerobic, mixed, or resistance) was moderately more effective than control interventions for treating depression, with exercise equally as effective as psychotherapy or pharmacotherapy [663]. The UK NICE Guidelines for depression recommend structured, supervised physical activity programs, three times a week (45 minutes to 1 hour duration) for at least 12 weeks [650].

There is much evidence suggesting that physical activity improves levels of depression and anxiety [664, 665], both of which are risk factors for, and have been associated with, AOD use [51, 666]. Despite this association, there is little research that has examined the role of exercise among people with comorbid depression and AOD use disorders specifically. A study examining the effects of an 8-week structured exercise program (treadmill and weight training), on depression and anxiety symptoms among newly abstinent methamphetamine users in treatment, found that more exercise was significantly associated with greater reductions in depression and anxiety symptoms, compared with the control group (health education sessions), and compared with fewer exercise sessions [233].

Another study, examining the effect of a 10-week, 30-minute, exercise program (incorporating walking/running, ball games, strength training) on quality of life in a sample of people attending residential AOD treatment for polydrug use, found a significant reduction in depression (from 78% to 36%) among those who completed the program [667]. This study highlights the difficulty involved in engaging comorbid populations in physical activity, which in general succeed in retaining only those with the fewest physical health problems [668]. However, the fact that 69% of participants completed the exercise component of this study does point to the feasibility of engaging and maintaining people with comorbid depression and AOD use disorders in programs incorporating physical activity [667].

A systematic review examining the effect of exercise-based interventions on AOD use found exercise was associated with overall improvements in depression [185]. Although these findings indicate that exercise is a potentially promising adjunctive treatment for people with comorbid depression, they also highlight the need for further well-conducted research to be undertaken in this area.

Complementary and alternative therapies

Yoga

Yoga is a complex mind–body intervention involving spiritual practice, physical activity, breathing exercises and meditation [669, 670]. Although the traditional goal of yoga is to unite body, mind, and spirit and achieve self-awareness, yoga has become a popular method of maintaining physical and mental health [669-671]. Yoga practice commonly involves postures to improve strength and flexibility, breathing exercises to focus the mind and assist with relaxation, and meditation to calm the mind [671]. Research has demonstrated that yoga can assist with the improvement of co-occurring mental health symptoms in patients with physical conditions such as cancer [672, 673], menopausal symptoms [674], and pain [675].

Several systematic reviews have been conducted to assess the efficacy of yoga as an intervention for depression. These studies have found limited to moderate support for short-term improvements in severity of depression in yoga with meditation-based practice (rather than exercise-based practice) [676-679]. Only one study has examined the effect of yoga breathing (Sudarshana Kriya Yoga) on depressive symptoms among people with alcohol dependence [680]. This study found that the yoga intervention was associated with reduced depressive symptoms compared to the control group. Although the effectiveness of yoga as a treatment for people with comorbid AOD and depressive disorders needs further investigation, these findings indicate that yoga may be considered as an additional treatment for clients with comorbid depression.

Omega-3

There has been much research conducted examining the relationship between omega-3 and depressive disorders, with some evidence that omega-3 fatty acids (primarily found in fish and seafood) are associated with lower rates of depression [681-688]. Although several studies support omega-3 supplementation as an antidepressant for people with depression alone, the role of omega-3 in people with comorbid AOD use and depression has not been rigorously examined.

Research that has included people with comorbid AOD use has been largely focused on aggression, anger, and co-occurring depression. Animal studies have found evidence of associations between omega-3 deficiencies and increased aggressive and depressive behaviours [689]. Beier and colleagues found reduced omega-3 levels among people with comorbid major depression and AOD use, indicating that omega-3 may be used as a therapeutic approach for people with depression and AOD use, and particularly those with aggressive symptoms [690]. Another placebo-controlled study of people with AOD abuse who had histories of aggression and legal problems found that anger improved with omega-3 supplementation [691, 692]. Other studies have also examined the relationship between omega-3

supplementation, depression, and co-occurring anger, aggression, hostility, and impulsivity, but have not included comorbid substance use [693-695]. Although these studies found that omega-3 supplementation improved depression and aggression [693, 694], Beier and colleagues suggest that AOD use (which was not measured) may have played an important underlying role [690].

St John's Wort

St John's Wort is the common name for the plant *Hypericum perforatum*, the extracts of which are commonly used to treat depression, sometimes in order to avoid the side-effects involved with prescription medication [696]. A systematic review of studies examining the efficacy of St John's Wort found significantly greater reductions in mild to moderate symptoms of depression among those taking St John's Wort compared to placebo [697]. However, the efficacy of St John's Wort compared to antidepressants is not known. The long-term side effects, particularly among pregnant women, are also unknown.

Although there is some evidence of efficacy in mild to moderate depression, the use of St John's Wort has been shown to have significant interactions with a range of other medications, including SSRIs and related drugs, oral contraceptives, some anticoagulants, and some cardiac medications [698]. Further, the use of St John's Wort among people with comorbid AOD and depressive disorders has not been examined. As such, AOD workers should ask their clients specifically about their use of St John's Wort and other complementary medicines, taking note of the potential for interactions between medications.

Summary

While these findings indicate that several psychological, pharmacological, and alternative approaches for the treatment of co-occurring depression and AOD use disorders appear promising, further research is required to establish which therapeutic approaches are particularly effective. It is suggested that clinical efforts be focused on the provision of client-centred, evidence-based treatment, taking into account the client's needs and preferences, in a collaborative partnership. Box 16 illustrates the continuation of case study D, following Jack after the identification of his comorbid depressive and AOD use disorder.

Box 16: Case study D: Treating comorbid depression and AOD use: Jack's story continued

Case study D: Treating comorbid depression and AOD use: Jack's story continued

Jack's revelations about his use of cannabis and alcohol led to a change in his treatment plan, and he realised for the first time that both alcohol and cannabis – alone or in combination – made his depression much worse. Jack said that there was a strong family history of depression; his father, one paternal uncle and his paternal grandfather, all experienced severe depression over the course of their lives, and his grandfather committed suicide in his early sixties. Jack went on to say that he had now realised that both he and his doctors had accepted a genetic causation of his recurrent depressive illness, without much thought being given to other factors such as AOD use.

With Jack's consent, the AOD worker spoke with his GP, psychologist, and psychiatrist to devise some treatment options for Jack. After presenting various options to Jack, it was decided that he would continue with his current antidepressant medication (which was working well so far), continue to see his psychologist weekly, and try attending some outpatient AOD group sessions for additional support. Jack was also made aware of the possibility of pharmacological therapies to help reduce his drinking, but he decided that he did not want to try medications at this stage. Jack continued with his antidepressant medication and seeing his psychologist, but decided after trying a few different support groups that it wasn't for him. Jack received regular ongoing monitoring of his physical health from his GP, who paid particular attention to Jack's liver function, respiratory health and blood pressure.

Box 16: Case study D: Treating comorbid depression and AOD use: Jack's story continued

Despite a few lapses, Jack progressed through treatment very well. Initially, he had some trouble abstaining from both alcohol and cannabis, but eventually stopped drinking and used cannabis only once per week. In planning his treatment, Jack had decided that he would take some time off work to concentrate on his mental health. After discussing his options with his psychologist, Jack decided to disclose the details of his condition, in confidence, to his employer who he had known for many years. Jack's manager was understanding and supportive, but he was also naturally concerned about Jack's return to work as several of the firm's clients were somewhat reliant on him.

In consultation with Jack's team of health care providers, it was agreed that he would have a short time off work and then return to work part-time, which in itself might be helpful to Jack in respect to improving his confidence and self-esteem.

Key points:

- People with comorbid disorders do not necessarily present in any obvious way. There is higher prevalence of older people who have continued to use AOD since cannabis and stimulants became more readily available in the 1960s and 1970s. The need for careful history taking regarding AOD use cannot be overemphasised.
- In some cases, mental health conditions may quickly respond to appropriate treatments. However, comorbid mental health and AOD use disorders present a numbers of challenges – in particular the need to address the need to maintain treatment gains in the long term (years rather than days or weeks).