Depression and anxiety

Summary

- Comorbid depression and anxiety disorders occur in up to 25% of general practice patients.
- About 85% of patients with depression have significant anxiety, and 90% of patients with anxiety disorder have depression.
- Symptomatology may initially seem vague and non-specific. A careful history and examination with relevant investigations should be used to make the diagnosis.
- Once the diagnosis is made, rating scales may identify illness severity and help in monitoring treatment progress.
- Both the depression disorder and the specific anxiety disorder require appropriate treatment.
- Psychological therapies, such as cognitive behaviour therapy, and antidepressants, occasionally augmented with antipsychotics, have proven benefit for treating both depression and anxiety.
- Benzodiazepines may help alleviate insomnia and anxiety but not depression. They have dependency and withdrawal issues for some people, and may increase the risk of falls in older people.
- Despite the availability of treatments, 40% of patients with depression or anxiety do not seek treatment, and of those who do, less than half are offered beneficial treatment.

Depression and anxiety disorders are among the most common illnesses in the community and in primary care. Patients with depression often have features of anxiety disorders, and those with anxiety disorders commonly also have depression. Both disorders may occur together, meeting criteria for both. It can be difficult to discriminate between them but it is important to identify and treat both illnesses, as they are associated with significant morbidity and mortality. General practitioners are well placed to identify and take a primary role in treatment of these illnesses, to facilitate better mental health outcomes.

Epidemiology

In Australia, the 12-month prevalence of anxiety disorders is 14.4% and of affective disorders, 6.2%.[1] It has been demonstrated that 39% of individuals with generalised anxiety disorder (GAD) also meet criteria for depression.[2] About 85% of patients with depression also experience significant symptoms of anxiety, while comorbid depression occurs in up to 90% of patients with anxiety disorders.[3] Considering anxiety and depression symptoms together in a "mixed anxiety-depressive disorder" has been proposed,[4] but it is useful to identify and institute effective treatment for each set of symptoms. They can occur in all age groups — almost 50% of older adults with 12-month history of GAD met criteria for lifetime major depressive disorder, while only 7.4% of those without GAD met these criteria.[5] Both anxiety and depression are associated with substance use disorder,[6] and about 7% of the affected population represent serious cases with high comorbidity.[7]

Up to 25% of the patients seen in general practice have comorbid anxiety and depression.[8] Though recognised in both rural and non-rural primary care, there is often a treatment gap, with patients undertreated for either or both disorders.[9] Patients with anxiety and/or depression are particularly likely to present with physical complaints rather than mental health symptoms,[10] and symptomatology may initially seem vague and non-specific.

Causal pathways

Developmentally, anxiety disorders are almost always the primary condition, with onset usually occurring in childhood or adolescence.[11] Comorbidity of anxiety and depression is explained mostly by a shared genetic vulnerability to both disorders, or by one disorder being an epiphenomenon of the other.[12]

Increased corticotropin-releasing factor in cerebrospinal fluid has been reported in both anxiety and depression, but other peptides or hormones of the hypothalamic–pituitary–adrenal axis are regulated differently in the two disorders.[13] More recently, neuroinflammatory, oxidative and nitrosative pathways have been implicated in depression and its comorbidities.[14] It is most likely that the first episode of depression in a person's life follows a psychosocial stressor. After three or more episodes, it becomes increasingly likely that subsequent episodes are spontaneous rather than following an external event.[15]

Impact and health care use

Comorbid depression and anxiety can increase impairment[16,17] and health care use,[18] compared with either disorder alone. Their co-occurrence is often associated with a poor prognosis[19] and significant detrimental impact on functioning in the workplace.[20] The number and severity of anxiety symptoms, rather than the specific anxiety diagnosis, correlate strongly with the persistence of subsequent depressive symptoms, and this relationship is stable over decades (Box 1).[21]

Many people do not seek treatment for anxiety and depression and, when they do, treatments are not always used effectively. Australian data suggest that 40% of people with current disorders did not seek treatment in the previous year and, of those who did, only 45% were offered a treatment that could be beneficial.[22] Despite the high prevalence of depression and anxiety, and notwithstanding Australia's universal health insurance scheme, service utilisation in this country is low. An Australian survey published in 2001 indicated that only 35% of people with a mental disorder had consulted a

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1 Relationship of anxiety and depression

Anxiety and depression, when combined:

- are more severe
- have a greater risk of suicide
- are more disabling
- are more resistant to treatment
- result in more psychological, physical, social and workplace impairment than either disorder alone ◆

health professional for a mental health problem during the previous year, but most had seen a GP for that disorder or for some other health reason.[23] In this setting, barriers to effective care were stated to be patient knowledge and physician competence.

Clinical recognition of depression and anxiety

It is important to delineate the specific depressive disorder and the specific anxiety disorder, as each may require different interventions. The most prevalent anxiety disorders in Australia are post-traumatic stress disorder (6.4%), social phobia (social anxiety disorder; 4.7%), agoraphobia (2.8%), GAD (2.7%), panic disorder (2.6%) and obsessive–compulsive disorder (1.9%). Of the population aged 16–85 years, 14.4% have an anxiety disorder. The prevalence of depression is 6.2%, with the prevalence of unipolar depressive episodes being 4.1%, dysthymia, 1.3%, and bipolar disorder, 1.8%.[1] Some patients have two or more disorders.

Diagnostic criteria are designed to distinguish between disorders, and exclude clinical features that are common to more than one. Thus, criteria for depression exclude common comorbid anxiety symptoms, and those for anxiety disorders exclude depressive symptoms. However, diagnostic criteria are not the same as clinical presentations. Some somatic symptoms that can occur with both depression and anxiety are outlined in Box 2.

It may be necessary to see a patient on several occasions to delineate his or her problems. If features of anxiety or depression are identified, features of the other disorder should always be sought. For example, if a patient is depressed, a clinician should ask, "With this illness, have you had symptoms like restlessness, irritability, impulsivity, palpitations [or other anxiety symptoms]?". If a patient is anxious, ask, "With this illness, have you had symptoms like feeling sad or numb, slowed up, loss of energy, a sense of hopelessness [or other depressive symptoms]?".

As treatments differ if the patient has bipolar depression, ask, "Have you ever had a period of time when you felt 'up' or 'high' or so full of energy, or irritable or angry, or full of yourself that you got into trouble, or that others thought you were not your usual self?" Bipolar disorder commonly presents as depression, even though the illness is defined by intermittent periods of mood elevation. Anxiety is common in patients with bipolar depression. Manic features that can mimic anxiety include decreased and restless sleep, distractibility, racing thoughts, irritability and agitation.

Despite data suggesting that the accuracy of depression recognition by non-psychiatrists is low,[24] the best remedy for this is not clear. Rating scales for depression and anxiety can be helpful, although most are designed to assess the severity of an already diagnosed illness rather than to make a new diagnosis.

A screening instrument that can be used to make a diagnosis and distinguish between illnesses, including unipolar and bipolar depression, is the Mini International Neuropsychiatric Interview.[25] Other instruments that can be used to identify the severity (but not the type) of depression include the Kessler Psychological Distress Scale,[26] the Hospital Anxiety and Depression Scale,[27] or the 12-item Somatic and Psychological Health Report questionnaire.[28] The Clinical Global Impression scale is a simple seven-point scale that can be used to monitor progress of treatment response.[29]

Treatment

In the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial, about half of the patients with major depressive disorder also had clinically meaningful levels of anxiety.[30] Remission was significantly less likely and took longer in the 53% of patients with anxious depression than in those with non-anxious depression. Side-effect frequency, intensity and burden, as well as the number of serious adverse events, were significantly greater and outcomes worse in the group with anxious depression.

There is a paucity of data on the treatment of patients with comorbid depression and anxiety, and clinical practice is therefore determined by treating individual anxiety and depressive disorders. There are also online resources that can help, including the Australian National University's MoodGYM (http://www.moodgym.anu.edu.au) and E-couch (http://www.ecouch.anu.edu.au), Swinburne University's Anxiety Online (http://www.anxietyonline.org.au), and information sites from *beyondblue* (http://www.beyondblue.org.au), Youthbeyondblue (http://www.youthbeyondblue.com) and the Black Dog Institute (http://www.blackdoginstitute.org.au).

Where the anxiety and depression stem from a general medical condition or complications of pharmacotherapy, clinicians should treat the medical disorder and review and

2 Somatic symptoms that can occur with anxiety and depression

General

- Fatigue and loss of energy, feeling slowed up or agitated and restless

Cognitive

- Poor attention and concentration, slow thinking, distractibility, impaired memory, indecisiveness

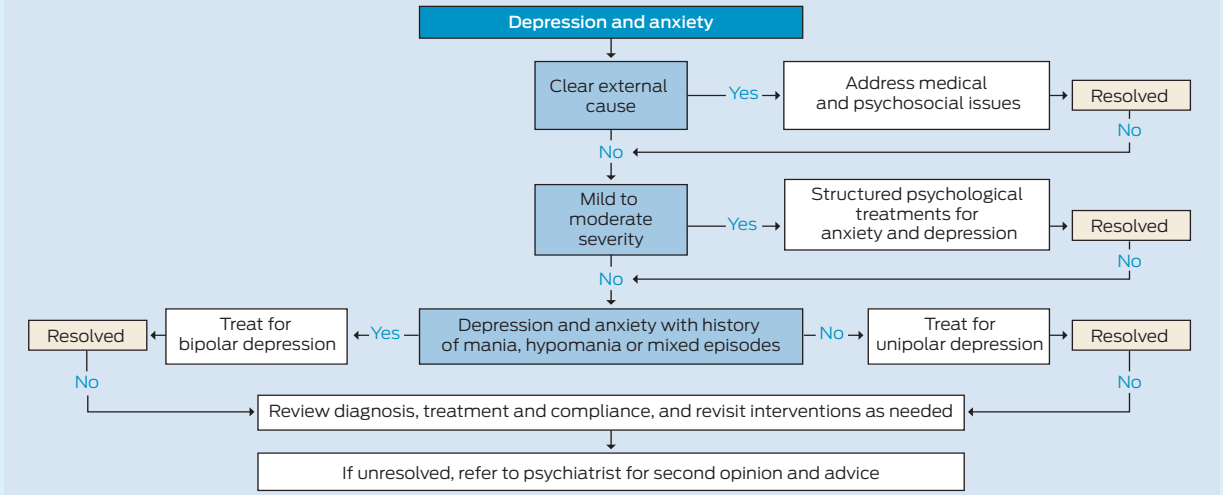
Psychological

- Apprehension, derealisation or depersonalisation, irritability, atypical anger

Somatic

- Musculoskeletal
  - Muscle aches and pains, muscle tension, headaches
- Gastrointestinal
  - Dry mouth, choking sensation, "churning stomach" sensation, nausea, vomiting, diarrhoea
- Cardiovascular
  - Palpitations, tachycardia, chest pain, flushing
- Respiratory
  - Shortness of breath, occasionally hyperventilation
- Neurological
  - Dizziness, vertigo, blurred vision, paraesthesia
- Genitourinary
  - Loss of sex drive, difficulties with micturition ◆

3 Flow chart for treating depression and anxiety



adjust pharmacotherapy as necessary. For most patients, there is no obvious medical aetiology.

Treatments for anxiety and depression can have substantial elements in common (Box 3). Initial steps are making the diagnosis, explaining symptomatology, and providing hope. Psychosocial interventions, including clinical support, education and rehabilitation, are valuable. For patients with mild to moderately severe depression and anxiety, structured psychological treatments, available under the federal government's "Better Access" scheme, will often suffice.[31]

For patients with more severe illness or those who do not respond to psychological interventions, pharmacotherapy is indicated. Pharmacotherapy particularly decreases over-activity of limbic structures of the brain (bottom-up effect), whereas psychotherapy tends to increase activity and recruitment of frontal areas (top-down effect).[32]

As most effective treatments for depression also have useful anti-anxiety effects, a pragmatic approach is to begin by treating the depression. Residual specific anxiety disorder symptoms can then be treated, with most responding to psychological interventions rather than additional pharmacotherapy.

Psychological treatments for depressive disorders

The psychological treatment with the greatest evidence base for depression is cognitive behaviour therapy (CBT).[33] CBT is a beneficial treatment that can be readily applied in medical practice. The principles involve educating the patient, teaching basic relaxation skills, and developing the patient's skills to identify, challenge and change maladaptive thoughts, feelings, perceptions and behaviour.[34] Systematic reviews and meta-analyses have shown evidence of efficacy in inpatients with depression[35] and those with chronic physical health problems.[36] A systematic review showed improved outcomes for patients by enhancing antidepressant therapy with non-pharmacological interventions.[37] Psychological treatments for depression are detailed elsewhere in this supplement (see Casey et al, *page 52*).[38]

Psychological treatments for anxiety disorders

Guidance regarding treatment of anxiety disorders can be found in a practical clinician guide and patient manuals,[39] and in an overview of management in general practice.[40] For GAD, a systematic review showed similar treatment effects for pharmacotherapy (odds ratio [OR] favouring active interventions over controls, 0.32; 95% CI, 0.18–0.54) and psychotherapy (OR, 0.33; 95% CI, 0.17–0.66).[41]

Pharmacotherapy for unipolar depression

Antidepressants are the mainstay of treating unipolar depression,[42] with present agents working mostly through serotonergic, noradrenergic, and dopaminergic receptors (see Chan et al, *page 44*).[43] An increase in prescribing of antidepressants in general practice in recent years coincided with the introduction of the Better Access initiative, which may have increased recognition of depression.[44] Antidepressant combinations may add to adverse events without necessarily providing therapeutic advantage, and some authorities do not support such use.[45] There is a new focus on normalising endogenous circadian rhythms in the treatment of depression and anxiety.[46] Bipolar depression needs different treatment (see Berk et al, *page 32*).[47]

Pharmacotherapy for anxiety disorders

Effective pharmacotherapy for depression will mostly reduce anxiety disorders as well. For some anxiety disorders, such as obsessive–compulsive disorder, higher doses of antidepressants are required than for depression. If anxiety continues, identify the specific disorder, then look to specific psychological interventions to treat the anxiety disorder, in addition to continuing antidepressants and/or mood-stabilising therapy. Engage specialist help if needed.

There has been a progressive move away from using benzodiazepines to treat anxiety because of problems with the actions of these agents and adverse events. As well as being anxiolytic, they are sedating, which can impair safety when patients are driving or using machinery; they also interact with alcohol. Their muscle relaxant effects can predispose to falls, especially in older people. There can be adverse effects on attention, concentration and memory. At higher doses, there is a greater risk of tolerance and dependency, as well as a risk of discontinuation effects, including possible seizures, when abruptly withdrawing benzodiazepines. Although some patients remain well and

in stable condition while taking low doses of these agents, the evidence is predominantly for their acute short-term use. Psychological interventions are generally preferable for sustained outcomes.

Low doses of atypical antipsychotic agents can reduce anxiety,[48] but there is a risk of tardive dyskinesia with long-term use, and metabolic problems are associated with some of these agents.

Antidepressants are the main options for long-term pharmacological treatment of anxiety disorders.[42] The choice of antidepressant depends on the prescribing doctor's knowledge of the medicine, a history of prior successful response to a particular agent by the patient or a close relative, or specific qualities of a particular medicine.

Conclusions

Comorbid depression and anxiety are common and affect up to a quarter of patients attending general practice. Screening for comorbidity is important, as such patients are at greater risk of substance misuse, have a worse response to treatment, are more likely to remain disabled, endure a greater burden of disease, and are more likely to use health services in general. There are effective treatments for specific disorders, but a paucity of data about treatment for anxiety and depression comorbidity. More than a third of patients with a mental disorder do not seek treatment, and almost half are offered treatments that may not be beneficial. This suggests the need for further public awareness and professional education that can enhance clinical practice, promoting better mental health outcomes.

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