

Depression and anxiety in patients with COPD

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Depression and anxiety are common in people with chronic obstructive pulmonary disease and are associated with significant distress, increased morbidity and mortality, and reduced functioning and quality of life.

Case scenario

Henry, aged 67 years, is a retired builder. He has worked hard all his life, and has seen himself as a strong, powerful and active person. Henry and his wife had been looking forward to an active retirement, with plans to travel and garden. A pack-a-day smoker since his mid-teens, Henry was diagnosed with chronic obstructive pulmonary disease (COPD) at age 50 and his respiratory function has steadily declined since then. He had been hospitalised on several occasions with exacerbations of COPD precipitated by infections. Due to breathlessness and fatigue, he is no longer able to play golf, work in his garden, go for walks with his wife, play with his grandchildren or travel. He gets breathless in day-to-day activities like walking to the gate to get the mail or showering, despite having attended a pulmonary rehabilitation program after his last hospital admission. Other medical problems include mild type 2 diabetes, hypertension, hypercholesterolaemia and osteoarthritis. He is underweight, and a recent bone scan identified moderately severe osteoporosis. He has no history of asthma.

Henry's current medication regimen includes:

- fluticasone furoate 100 mcg, umeclidinium bromide 62.5 mcg and vilanterol trifenate 25 mcg combined, one inhalation daily
- irbesartan, 150 mg in the morning
- salbutamol metered-dose inhaler, two to four inhalations via spacer as needed
- rosuvastatin, 10 mg daily
- metformin, 1000 mg twice daily
- calcium, 1200 mg in the morning
- cholecalciferol, 1000 IU in the morning
- paracetamol, 665 mg three times daily as needed
- celecoxib, 100 mg twice daily
- omeprazole, 20 mg in the morning
- temazepam, 20 mg at night

Since retiring at age 60 years, Henry has become increasingly withdrawn and low in mood. He sleeps poorly and is tired during the day. His appetite and diet are poor and he sometimes says that he wishes he could go to sleep and not wake up. He has little pleasure in life and sees no hope for the future. He feels anxious, particularly after taking his medications or after exertion. He spends his days at home watching



Key points

- There is a bidirectional relationship between depression and medical illness.
- Comorbid depression and anxiety are associated with more severe medical illness, increased morbidity and mortality, increased functional disability and poorer quality of life.
- Comorbid depression is associated with increased presentations to healthcare services and increased costs of care.
- Treating depression and anxiety may reverse this cascade.
- All patients with obstructive pulmonary disease should be screened for depression and anxiety.
- Recommended treatments include antidepressants, psychotherapy and pulmonary rehabilitation, although evidence is limited.
- Any other medications or medical conditions that might be contributing to depression should be identified and managed.

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1. Depression criteria³

For a diagnosis of depression, according to DSM-5, at least five of the following symptoms need to have been present during the same two-week period and must include diminished pleasure or depressed mood:

- Depressed mood OR
- Diminished interest or loss of pleasure in almost all activities (anhedonia) and at least three of:
 - significant weight change or appetite disturbance
 - sleep disturbance (insomnia or hypersomnia)
 - psychomotor agitation or retardation
 - fatigue or loss of energy
 - feelings of worthlessness
 - diminished ability to think or concentrate, or indecisiveness
 - recurrent thoughts of death, recurrent suicidal ideation without a specific plan or a suicide attempt or specific plan for committing suicide.
- The above symptoms cause significant distress or impairment in social, occupation or other important areas of functioning
- The symptoms are not attributable to the physiological effects of a substance (e.g. a drug of abuse, a medication) or another medical condition
- The disturbance is not better explained by another mental disorder and there has never been a manic episode or a hypomanic episode

television. His most recent lung function test showed a low forced expiratory volume in one second (FEV₁) of 32% of predicted and a forced vital capacity (FVC) of 70% of predicted. The FEV₁/FVC ratio was 0.50, indicating a significant degree of airflow obstruction.

At his next admission, Henry is noted to be low in mood. He seems amotivated (lacking in motivation) to engage in pulmonary rehabilitation and appears to have little understanding of his illness or its treatments. He concedes he is depressed but says: 'Wouldn't you be? There is nothing anyone can do about it.' He reluctantly agrees to talk

to the Consultation Liaison Psychiatry Service.

The psychiatrist notes that Henry looks depressed and despondent, appearing older than his years with chronic poor health but strong family support. He appears tense and restless. He has not found meaningful activity since retiring and now feels worthless. He describes pervasive low mood, guilt for not looking after his health better, hopelessness and helplessness about his capacity to improve his health and engage in the activities he had hoped would fill his retirement. He denies thoughts of harming himself but frequently thinks about dying. He feels anxious when he leaves the house and when he is short of breath, and on several occasions has felt so bad that he feared he might collapse or die. He is embarrassed to be seen by his friends and family, feeling ashamed of his weakness and his productive cough. He misses being strong and capable and feels humiliated by his current compromised health status and need for care by his wife, Lily. His wife confirms that he has been miserable for some time. He worries constantly about 'everything', which makes it difficult for him to concentrate. Lily says she is at her wits end, as Henry won't try to get better and won't engage with even the activities he can manage.

Commentary

Diagnosis

Chronic physical illness

Henry has well-established, severe COPD which, as is common, is complicated by a number of other medical conditions including type 2 diabetes, hypertension, hypercholesterolaemia, obesity, osteoarthritis and osteoporosis.^{1,2} He is experiencing significant functional impairment and his quality of life is low. He manages his health poorly with low adherence to medication, diet and exercise recommendations, and has limited understanding of his health despite having completed a pulmonary rehabilitation program. His illness is having a deleterious effect on his family.

Psychological illness

In addition, Henry fulfils the criteria for DSM-5 major depressive disorder (Box 1).³

Major depressive disorder is formally defined by pervasive low mood, feelings of worthlessness, and loss of pleasure (anhedonia, or inability to feel pleasure in normally pleasurable activities) occurring every day for at least two weeks. It is commonly associated with other neurovegetative symptoms (weight loss, sleep disturbance, psychomotor change) and cognitive symptoms (poor attention and memory, feelings of guilt, suicidal thoughts).

He feels anxious when he leaves the house and when he is short of breath, and on several occasions has felt so bad that he feared he might collapse or die

Henry also experiences significant anxiety, which is common in the context of depression and COPD. Such anxiety may present as feeling tense and worried, being restless, agitated and panicky, and having a sense of dread or a fear of losing control or dying, which can lead to avoidant behaviour (e.g. not leaving the house, avoiding social situations). People with chronic illness are commonly fearful about medical symptoms which, while understandable, may be exaggerated in people with dysfunctional levels of anxiety. Dyspnoea and palpitation may be misinterpreted by the mind and body as a catastrophic threat by the mind and body, generating anxiety and panic that fuel a positively reinforcing cycle of dysfunction.^{4,5} People who have experienced medical crises may also experience symptoms consistent with post-traumatic stress.⁶ The DSM-5 defines a number of distinct anxiety disorders. Henry has symptoms consistent with generalised anxiety disorder (Box 2) and his history suggests that he has experienced occasional panic attacks (Box 3). He also displays some features of social anxiety (worry about negative evaluation by others) and anxiety disorder due to a medical condition or substance.³ As these symptoms have only occurred in the context of major depression and COPD (and other chronic illness), they are not diagnosed separately. Pragmatically, it is important to recognise

2. Generalised anxiety disorder criteria³

For a diagnosis of generalised anxiety disorder, according to DSM-5, the following symptoms need to be present:

- Excessive anxiety and worry occurring more days than not for at least six months, about a number of events or activities
- The person finds it difficult to control the worry
- The anxiety and worry are associated with three or more of the following six symptoms:
 - restlessness or feeling keyed up or on edge
 - being easily fatigued
 - difficulty concentrating or mind going blank
 - irritability
 - muscle tension
 - sleep disturbance
- The anxiety, worry or physical symptoms cause clinically significant distress or impairment in social, occupation or other important areas of functioning
- The disturbance is not attributable to the physiological effects of a substance or another medical condition
- The disturbance is not better explained by another mental disorder

that Henry has significant and debilitating comorbid anxiety symptoms with a number of potential contributing factors and clinical manifestations.

In the setting of complex medical illness, the overlap of symptoms of anxiety and depression with those of the chronic illness(es) can make the attribution of symptoms to particular diagnoses difficult and not always feasible or useful. For instance, fatigue, poor sleep and weight loss are features of both COPD and depression. The key to identifying significant depressive disorder is recognising the key symptoms of enduring low mood and anhedonia. At the same time, the contribution of 'physiological effects of a substance or medical condition' to depression and anxiety symptoms must

be considered, as there may be treatable and possibly undiagnosed medical conditions manifesting as psychological symptoms. For instance, corticosteroids are recognised to elevate or depress mood and cause symptoms of anxiety and insomnia.⁷ Beta-2 agonists can cause insomnia as well as temporary tachycardia, tremor and increased breathlessness, which contribute to a feeling of anxiety.⁸ Other physical conditions that may manifest psychological symptoms include thyroid disease, vitamin deficiency, early dementia, Parkinson's disease, autoimmune disorder or an underlying malignancy.

For a differential diagnosis, it is important to consider whether the symptoms of depression that are apparent in the acute setting are a temporary dip in mood in the context of a medical crisis or if they are of longer standing. The collateral history provided by the patient, a family member or GP may help to establish the longevity and severity of the person's symptoms. In the case of symptoms of brief duration, a diagnosis of adjustment disorder with depressed mood might be made. If less than five criteria for depression are present, a diagnosis of minor depressive disorder is made as long as depressed mood and anhedonia are present.

Discussion

Depression and anxiety are common comorbidities in people with chronic illness and occur in up to 80% of individuals, with categorical depressive and anxiety disorders occurring in up to 55%.^{9-12,23} There is a well-recognised bidirectional relationship between depression and anxiety, and COPD, as well as with other chronic medical conditions, including type 2 diabetes, dementia, stroke, coronary heart disease, cancer, obesity and hypertension.^{13,14} Comorbid depression and anxiety predict overall higher morbidity and mortality with greater functional impairment and medication nonadherence, poorer engagement in lifestyle modifications such as smoking cessation, weight loss or exercise programs, and increased illness exacerbations and healthcare use.^{13,15-19} Conversely, a diagnosis of chronic illness increases the likelihood of developing depression and anxiety. Furthermore, COPD may be

3. Panic attacks and panic disorder

Panic attacks are abrupt surges of intense fear or intense discomfort that reach a peak within minutes and are accompanied by physical symptoms including palpitations, sweating, trembling or shaking, dyspnoea, feeling of choking, chest pain, dizziness or light-headedness, chills or heat sensations, numbness or tingling, feelings of unreality, fear of losing control or of dying and cognitive symptoms.

- The symptoms are self-limiting but intensely unpleasant and often lead to avoidance of the situations in which panic occurred
- The symptoms may occur, as in this case, in the context of another mental disorder or in isolation

Panic disorder is diagnosed if panic symptoms are associated with a persistent worry about having panic attacks and avoidance behaviours.

associated with particularly high rates of depression and anxiety compared with other chronic illnesses.¹⁰

A range of biopsychosocial factors have been identified as contributing to the high rates of depression and anxiety in the context of COPD. COPD is associated with a gradual increase in physical debilitation linked to chronic cough, reduced capacity for physical exertion due to dyspnoea, fatigue and frailty. Reduced mobility limits independence, and thus capacity to engage in social activities. There may also be grief over loss of health, lifestyle and employment.²⁰ Many patients experience feelings of shame and guilt as the illness is widely considered by patients and others to be self-induced.²¹ Discomfort with altered appearance and sense of self can contribute to avoidance of social contacts. Chronic cough and sputum production may be perceived as embarrassing and off-putting to others.²²

Underdiagnosis of depression and anxiety

Less than one-third of patients with COPD and comorbid depression and anxiety are

estimated as receiving appropriate treatment.²³ Depression and anxiety may be under-recognised for a number of reasons including: the salience of medical symptoms during consultations; failure to recognise symptoms as reflecting anxiety or depression rather than COPD or other medical comorbidities; failure to ask about or systematically screen for mood symptoms, which may relate to a perceived lack of skill or discomfort in asking about psychological distress; and patients not recognising their symptoms as anxiety or depression, or feeling embarrassed to ask for help, and assuming that psychological distress is inevitable in the context of chronic illness.²

Other assessments and investigations

As part of a comprehensive assessment of low mood and anxiety in the context of COPD and other chronic illness, it is important to screen for medical conditions that may be contributing to symptoms. These include thyroid function, obstructive sleep apnoea (OSA), dementia, cerebrovascular disease, Parkinson's disease, diabetes, chronic pain, renal and liver function and anaemia – all of which may present with or contribute to low mood.

In this case, type 2 diabetes was already

identified. Thyroid, renal and liver function were normal, and a full blood count revealed no abnormalities. Brief cognitive testing revealed no evidence of cognitive impairment suggestive of undiagnosed dementia and an MRI scan revealed white matter changes consistent with age.

Given his daytime sleepiness, screening for OSA was undertaken. Henry's wife confirmed that he was a heavy snorer and she had noticed him stop breathing for short periods at night followed by gasping for air. He scored eight on the STOP-Bang questionnaire and 12 on the Epworth Sleepiness Scale, confirming that he is at high risk for OSH.^{24,25} After discharge he underwent a sleep study, which showed severe OSA with an average apnoea-hypopnoea index of 35 and oxygen saturation to a nadir of 75%.

Guidelines and management

The management of depression and anxiety in the context of complex comorbidity requires a multimodal, collaborative approach that addresses all contributing factors and acknowledges their interdependence.^{13,14}

The Australian COPDX guidelines identify the treatment of anxiety and depression as a key component, advocating screening for anxiety and depression using the

Hospital Anxiety and Depressions Scale (HADS) or the more comprehensive Patient Health Questionnaire (PHQ), as well as referral to mental health services for ongoing management. They also note the role of pulmonary rehabilitation in encouraging engagement with support groups for patients and their families, which may provide emotional support, social interaction, knowledge and strategies for coping. The Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease 2017 Report GOLD Executive Summary emphasises the identification and treatment of the disease's comorbidities but notes only that 'anxiety and depression are both associated with a poor prognosis'.²⁶⁻²⁹

While the lack of detailed mental health recommendations in COPD guidelines has been attributed to the paucity of quality evidence supporting treatment, some experts are calling for greater responsibility on the part of nonmental health clinicians for identifying and treating anxiety and depression symptoms in patients, given their prevalence and impact, and the limited access to mental health professionals, and greater acceptability of nonmental health service interventions to some patients.^{2,30,31} Although delivery of cognitive behavioural therapy (CBT) and other psychotherapies require

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Table. The biopsychosocial and lifestyle (BPSL) approach to managing depression as applied to Henry*

Biological	Psychological	Social	Lifestyle
Potential causes			
- Chronic obstructive pulmonary disease - Respiratory infections - Osteoporosis - Osteoarthritis - Obstructive sleep apnoea - Long-acting beta agonists - Corticosteroids - Poor adherence to medication - Poor puffer technique - Muscle wasting - Smoking	- Grief regarding loss of lifestyle and identity - Depressed mood with a sense of worthlessness and hopelessness - Fear of not being able to breathe - Panic - Shame and embarrassment leading to social avoidance - Unhelpful beliefs about his illness - Poor sense of being able to manage his illness - Low adaptability and resilience	- Social isolation - Lack of meaningful activity - Retirement - Financial strain - Relationship strain	- Exercise limited by pain, obesity, shortness of breath, low energy and motivation - Excessive sedentary behaviour - Poor diet - Sleep disturbance
Possible treatments			
Short term			
- Antidepressants - Minimise medications contributing to depression and anxiety - Optimise chronic obstructive pulmonary disease treatment - Improve puffer technique	- Start psychotherapy with patient and family psychoeducation - Explain role of depression and anxiety - Instil hope	Caregiver support	Nutritional supplements
Medium term			
- Pulmonary rehabilitation - Manage obstructive sleep apnoea - Improve medication adherence, e.g. Webster-paks, reminders	- Pulmonary rehabilitation - Cognitive behavioural therapy	- Pulmonary rehabilitation - Education about physical and psychological illnesses - Family and friends - Community groups - Housing modifications - Financial support - Formal support groups	- Pulmonary rehabilitation - Smoking cessation - Sleep intervention - Diet and exercise
Longer term			
Influenza and pneumococcal vaccine	Ongoing psychotherapy/psychological support	As above	- Diet and exercise - Smoking cessation

*Modified from the Royal Australian and New Zealand College of Psychiatrists BPSL model.³²

considerable training, they do not always need to be delivered by a clinical psychologist to achieve positive outcomes for patients with COPD, at least for those with less severe or less complex depression or anxiety.³¹

The Royal Australian and New Zealand College of Psychiatrists Clinical Practice Guidelines for Mood Disorders advocate a holistic approach to the management of depression, which recognises the contributing biological, psychological, social and

lifestyle (BPSL) factors in a particular patient.³² This approach is helpful in discussions with the patient and their family, as well as with other clinicians, as it highlights the interrelatedness of the patient's various issues and provides a framework for management (Table).

The primary aim of treatment is to improve mood and restore a sense of hope and enjoyment in life. The choice of first-line interventions depends on the severity of

symptoms and clinical judgement of priorities, ideally determined in discussion with the patient, their family and key clinicians. It is important to note that the patient's capacity to make decisions about their treatment may be compromised by physical and/or psychological illness. Short-term symptomatic improvements in COPD symptoms and pain may instil hope that improvement in quality of life is possible. Education about medications, pulmonary

4. Treatment considerations for patients with depression or anxiety

- Respiratory rehabilitation
- Smoking cessation
- Exercise program
- Involve partner and family where possible
- Promote what is possible rather than what is not
- Psycho- and respiratory-education
- Cognitive behavioural therapy
- Medication
- Address sleep issues
- Treat obstructive sleep apnoea

rehabilitation and the impact of depression and anxiety symptoms can help to restore a sense of control and a way forward. In the medium and longer term, treatments targeting specific symptoms and underlying causes can be instigated as tolerated. These would include management of depression, anxiety and insomnia, as well as engagement in rehabilitation if available, with the aim of improving exercise tolerance, reducing dyspnoea, increasing mobility, cessation of smoking and increasing social supports including for carers. It may also be necessary to address financial concerns and modifications to the home environment to overcome barriers to improved function. All these interventions may directly or indirectly impact on mood and wellbeing.

The evidence base for treatment of depression and anxiety in the context of COPD is limited, with most treatment decisions made on the basis of evidence in patients without COPD. Recent systematic reviews concluded that there was inadequate evidence to support pharmacotherapy (antidepressants) for depression or anxiety in patients with COPD.^{33,34} Support for CBT in the treatment of depression and anxiety is stronger but still limited.^{34,35} Pulmonary rehabilitation and exercise programs are recognised to have significant benefits on depression and anxiety

symptoms as well as improving exercise tolerance and quality of life.³⁶ There is evidence that exercise programs also have a positive effect on depressed mood and anxiety symptoms (Box 4).^{36,37}

Despite the absence of convincing evidence, antidepressants, in particular selective serotonin reuptake inhibitors, remain widely used in patients with COPD who are depressed and anxious. The availability of CBT and pulmonary rehabilitation is limited whereas selective serotonin reuptake inhibitors are inexpensive and considered relatively safe, bearing in mind the potential for interactions with existing medications, their side effect profile and the acceptability of treatment.

Benzodiazepines should be avoided in patients with severe COPD or OSA as sedation can depress respiratory effort and increase the risk of falls in the elderly.³⁸ Benzodiazepines were linked to increased mortality in a cohort of 2249 patients with very severe COPD starting oxygen therapy (hazard ratio, 1.21; 95% confidence interval, 1.05-1.39), although lower dose opioids (equivalent to less than 30 mg oral morphine a day) were not and may help with breathlessness. There is concern about the increased risk of falls, which is a particular issue in the setting of osteoporosis.³⁹

Case outcome

After discussing the association between COPD and depression and anxiety, Henry was started on sertraline as it is well tolerated and not associated with drug interactions. He was referred to outpatient pulmonary rehabilitation, which involved an exercise program, education and support. He attended 10 sessions of CBT to address unhelpful cognitions, his fear and over-interpretation of physical symptoms and to reduce avoidance of social situations. Medication adherence was improved by explaining the role of each drug, training in inhaler technique and use of a blister pack. He began re-engaging with family and friends, finding activities that he could enjoy

with them. He also cut down and finally ceased smoking, which gave him a sense of satisfaction. With some struggle, he began treatment for OSA, which improved his daytime alertness, energy levels and sleep quality. His depression and anxiety scores at six- and 12-months' follow up were significantly reduced and his mobility and exercise tolerance increased with engagement in regular physical activity and exercise. The purchase of a mobility scooter helped him to regain some independence over longer distances and overall his quality of life improved.

Conclusion

COPD is a complex illness often associated with multiple comorbidities, including high rates of depression and anxiety. Psychological symptoms are debilitating and distressing of themselves, and are associated with poorer quality of life and higher morbidity and mortality. Despite this, depression and anxiety are under-recognised and undertreated and there remains a lack of evidence to support treatment choices. Current guidelines recommend a comprehensive biopsychosocial-lifestyle approach, which acknowledges the complex interactions between physical and psychological symptoms and might include pharmacological and psychosocial therapies and, importantly, pulmonary rehabilitation. Screening for anxiety and depression symptoms should be routine for patients with COPD.

RMT

References

A list of references is included in the online version of this article (www.respiratorymedicinetoday.com.au).

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