

Making sense of the complex depressed patient – 1

Medical illness, including effects of drugs and alcohol

Depression takes various forms in people with medical illness including normal experience, personality traits, adjustment reactions/disorders and clinical disorders. Differing approaches are required to treat these and enhance the patient's ability to cope with the medical illness and other comorbidities.

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Depression is viewed as a major public health challenge for the twenty-first century and there has been considerable 'consciousness raising' over the past decade. Depression is now seen as often fitting a chronic disease model and there are many factors that complicate presentation and course.

Analysis of data from the National Survey of Mental Health and Well-being carried out in 1997 shows current (30-day) prevalence rates of major depression of 3.2% in Australia, with unemployment and smoking status, presence and number of medical illnesses, followed by being in midlife,

previously married and female all as independent risk factors.¹ There are higher rates of depression in the presence of respiratory disease, cardiovascular and vascular disease, Parkinson's disease, diabetes, renal disease, cancers, HIV infection, smoking, alcohol use and illicit drug use.^{1,2}

Depression may take many forms, particularly in people with a medical illness, and its manifestation is influenced by the patient's temperament and personality style. The depression may become chronic, and can be part of bipolar disorder. This article, the first in a series of three on the complex

IN SUMMARY

- Depression in the context of medical illness is often viewed as being 'understandable' and not requiring treatment. However, the physical illness and its treatment can contribute to the precipitation of clinical depression.
- Psychotherapy and allied health interventions (including clinical psychology, occupational therapy and physiotherapy) should be considered as well as antidepressants when managing depression in patients with medical illnesses.
- When choosing medications, the target symptoms and the side effect profiles of the medications should be considered.
- Dual action antidepressants, which are both serotonergic and noradrenergic, can improve depression, insomnia and pain tolerance.
- In those patients with multiple medical, psychiatric and substance use comorbidities, ceasing substance use can assist mental as well as physical health.

depressed patient, discusses the types of depression seen in people with a medical illness and also approaches to management. The second and third articles, to be published in future issues of *Medicine Today*, will discuss the influence of patients' temperamental and personality factors on the choice of management and the likely problems, and the assessment and management of patients with melancholic depression, including those with bipolar disorder.

Depression and medical illness

Depression in patients with a medical illness can take the form of 'normal' reactive depressive symptoms, including demoralisation and grief.³ However, there can be interactions between physical illness and depression, including symptoms being shared between depression and medical illness (for example, tiredness, anorexia and insomnia) and depression arising as a prodrome to, or consequence of, the medical illness. Many serious medical illnesses are accompanied by some depressive symptoms, and some medical illnesses (including malignancy, painful syndromes, endocrine disorders and some viral disorders) and some medications are

depressogenic, although this effect may be masked by somatising behaviour.⁴ Illnesses and medications that may lead to depression are listed in Table 1. Fact sheets for patients about depression in a variety of medical illnesses are available on the beyondblue website (see the box on page 43).

Table 1. Illnesses and medications leading to depression³

<p>Neurological and intracerebral illnesses</p> <p>Small and large vessel cerebrovascular disease</p> <p>Stroke</p> <p>Arteriovenous malformations</p> <p>Parkinson's disease</p> <p>Huntington's disease</p> <p>Tumours</p> <p>Autoimmune disease (e.g. systemic lupus erythematosus), especially those leading to cerebral vasculitis</p> <p>Early dementia from any cause</p> <p>Occult neoplasms</p> <p>Abdominal cancers particularly (e.g. pancreatic cancer)</p> <p>Small cell carcinoma of lung</p> <p>Tumours in frontal lobes</p>	<p>Medications*</p> <p>Antihypertensives</p> <p>Beta blockers</p> <p>Cimetidine</p> <p>Corticosteroids</p> <p>Oral contraceptives</p> <p>Interferon</p> <p>Isotretinoin</p> <p>Vinblastine</p> <p>Vincristine</p> <p>Most tranquillisers, sedatives and antipsychotic drugs</p> <p>Anti-inflammatory agents</p> <p>Substance abuse</p> <p>Amphetamines/cocaine</p> <p>Other stimulant dependence</p> <p>Nicotine dependence</p> <p>Alcohol abuse and dependence</p> <p>Sedative abuse and dependence</p>	<p>Infections</p> <p>Cerebral infection (bacterial or viral)</p> <p>Endocrine disorders</p> <p>Addison's disease</p> <p>Cushing's syndrome</p> <p>Thyroid disease</p> <p>Diabetes (type 1 and type 2)</p> <p>Cardiac, respiratory, renal illnesses</p> <p>Heart failure</p> <p>Myocardial infarct</p> <p>Chronic respiratory disease</p> <p>Renal failure</p> <p>* Not a comprehensive list</p>
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Table 2. Factors complicating depression in patients with medical illness

- A wide range of illnesses cause symptoms or signs that precipitate depressive symptoms (see Table 1); some also mimic depression (e.g. organ failure, frontal lobe disease, hypothyroidism, Parkinson's disease)
- Comorbid alcohol/substance/analgesic/sedative abuse or dependence, nicotine dependence
- Presence of delirium (especially hypoactive delirium) and/or dementia
- Medications that precipitate, mimic or mask depression or interact with psychoactive medications
- 'Unfinished emotional business', especially grief and anger
- Underlying personality traits, personality disorder
- Presence of anxiety disorders and somatising behaviour
- Side effects of prescribed medications and interactions between medications used to treat medical illness

There is also a 'vicious cycle' whereby depression is associated with worsening of the index medical illness, with greater morbidity in turn leading to increased severity of depression. Suicidal ideation occurs generally in medically ill patients who also fulfil criteria for major depression, and often diminishes or disappears with assertive treatment of the depressive disorder.

Clearly substance abuse and personality factors also play a part. Dependent users of nicotine and alcohol have higher rates of depression, and many of the common depressogenic medical illnesses and nicotine and/or alcohol use adversely affect each other. Dependent smokers have higher rates of suicidal ideation than non-smokers, and these rates increase with the number of cigarettes smoked (smokers of

25 or more cigarettes a day have four times the rates of suicidal ideation of non-smokers).⁵ Compounding factors include the effects of abuse of, dependence on and withdrawal from alcohol, cannabis, nicotine, cocaine, amphetamines and other recreational drugs, the effects of analgesics and sedative/hypnotic drugs, and the side effects of medications, particularly in the context of multiple medications.

Two parallel agendas Type and severity of depression

The type and severity of the depression need to be determined. The comment, 'of course the patient is feeling like that when they're so ill', is often heard. Additionally, depression may be masked by somatising behaviour⁴ and some disorders can mimic depression (including hypoactive delirium and frontal dementia). Although it is normal for people to feel sad and distressed about the prospect of dealing with a serious medical illness, pointers to clinical depression in such people include their feeling consistently depressed and having lack of reactivity, lowered self-esteem and increased self-blame, hopelessness and rumination (stewing over things).⁶

Some criteria for major depression (such as changes in sleep, appetite and concentration) are less discriminating in the presence of any of the many medical illnesses where they are also common features.^{6,7} As a rule of thumb, when patients become depressed, they experience lowered self-esteem and increased self-criticism, guilty thoughts and tendency to ruminate or stew, and become preoccupied with hopelessness. They may develop psychomotor changes (indicative of melancholic depression) and may even become psychotic. These features do not occur in nondepressed people with medical illness, who may still be fatigued and experience appetite or sleep disturbance, demoralisation, grief and medical or medication complications due to their medical condition.

It is often possible to distinguish

between depressed and nondepressed patients with medical illness. The DMI-10 (10-item Depression in the Mentally Ill Scale) or 12-item SPHERE (Somatic and Psychological Health Report) plus a disability measure such as the SF-12 (the Short-Form 12-Item Health Survey) can be helpful here.⁶⁻⁸ The version of SPHERE on the beyondblue website also has behavioural items indicating disability (see page 43). In cases where there is doubt, the judicious trial of an antidepressant is appropriate. An information sheet for GPs about antidepressant drug prescription is available on the Black Dog Institute website (see the box on page 43).

Complicating illnesses and medications

The other agenda is consider the presence of a range of medical illnesses and their treatments that can complicate the course of depression by precipitating onset, prolonging course, affecting impact of antidepressants and mimicking depression (Table 2).

People with histories of substance abuse or dependence are likely to have further complications of both their medical condition and any depression. Such histories include nicotine dependence or abuse, and dependence on alcohol, prescribed or illicit drugs (including sedatives/hypnotics, stimulants and other psychoactive agents).

Assessing a patient with melancholic depression

As later onset melancholic major depression is associated with cerebrovascular disease, there are likely to be increased rates of melancholic depression in people with medical illnesses predisposing to vascular disease, Parkinson's disease and some malignancies. An information sheet for GPs about melancholic depression is available on the Black Dog Institute website (see page 43). (The third article in this series will discuss melancholic depression in more depth.)

Table 3. Assessing depression in patients with medical illness

Patient feature	Assessment
Does the patient have an anxiety and/or depressive disorder?	Exclude delirium, changes due to medical illness, intoxication – self-report instruments such as DMI-10 and SPHERE can assist in identification of depression types ^{6,7} Exclude delirium and dementia, especially frontal dementia, as both can be interpreted as depression Check orientation, ask relatives about recent behaviour, ask patient to draw clock face, frontal lobe testing
What type of anxiety?	Check whether anxiety is episodic or part of a personality style, and whether it predated the illness
Is there a past history of depression? Is this episode similar to previous episodes?	Consider gathering other details
Is there a history of regular use of nicotine, alcohol or other substances?	Assess history and degree of reliance on these substances – all may affect depression
Have there been any changes in medication leading to drug interactions? Are there increased side effects?	Check drug interactions (consult pharmacist or clinical pharmacologist), treat as appropriate
What sort of sleep problems are there? Is there sleep apnoea?	Consider sleep hygiene, assess and treat sleep apnoea
Is there evidence of malabsorption or dietary problems?	Dietary problems will resolve when malabsorption is treated May lead to vitamin B ₁₂ and/or folate deficiency
Is there significant pain?	Pain is a potent source of inactivity and helplessness and can be a powerful precipitant of depressive episodes Pain and analgesics can maintain depression
Is there evidence of somatising behaviour?	Consider what is being communicated by the behaviour

The following questions can be useful in identifying the symptoms of melancholic depression:⁹

- Are you stewing over things?
- Do you still read the newspaper or watch TV?
- How do you spend your day?
- Do you still enjoy hobbies/children/grandchildren?
- Do you feel worse in the morning?
- How do you sleep?
- Do you wake early in the morning?
- Can you be cheered up?
- What lifts your mood?

The characteristic ‘psychomotor signs’ of melancholic depression of physical and mental agitation and slowing and the associated cognitive changes can be affected by some medical illness but are usually

still recognisable. Again, if in doubt, an antidepressant can be trialled. A guide to determining the appropriate assessment of depression in patients with medical illness is given in Table 3.

Management of depression in the medically ill

It is important to consider psychological interventions and physiotherapy as well as the use of antidepressants when managing depression in patients with medical illness. A guide to determining the appropriate intervention is given in Table 4.

Patient-centred counselling

Patients with a medical illness and depression are often frightened and overwhelmed by the combination of physical

and emotional factors. They may also be dealing with a series of clinicians. It is important to help them streamline the process, learn to self-manage, ask for help and work collaboratively with the medical teams.

It is necessary to be aware of and understand the meaning of the illness to the patient and to provide counselling for the issues that arise. Patients often feel trapped, immobilised, hopeless and helpless – all these feelings are potent in precipitating and maintaining depressive episodes and may reawaken memories from similar situations in the past. Patients with these emotions will benefit from counselling and support. There may also be ‘unfinished business’, especially involving suppressed grief and anger, which is

continued

Table 4. Managing depression in patients with medical illness

Patient feature	Intervention
Is there an unresolved loss?	Consider grief counselling or psychotherapy
Are there current stressors precipitating depression or impeding recovery?	Offer stress management skills, relaxation skills, problem solving, CBT approaches, family support
Is there new anxiety/panic due to breathlessness?	Use specific techniques to improve posture and breathing control, sleep quality, overcome panic
Is there decreased mobility?	Techniques to improve mobility using a rehabilitation framework can be useful; may involve physiotherapy and occupational therapy
Are there long-term interpersonal difficulties?	Identify problems, offer interpersonal, relationship and family therapy where needed; longer term psychotherapy may be required
Are there issues of self-blame about the patient's illness?	Clarify misunderstandings, guilt issues, 'unfinished psychological business'
Are there ongoing undue concerns with health? Is there somatising behaviour? Is there a long history of health anxiety or is it recent?	Use reattribution techniques to illustrate relation between psychological issues and body function ⁴ Consider CBT for longstanding problems ²
Use of antidepressants	
Which antidepressant to use?	Consider target symptoms, past history, risk of overdose, medical history, current medications and past sensitivities and interactions
Is there worrying, ruminations, obsessional thinking or rituals?	Consider using an SSRI (generally sertraline, citalopram and escitalopram have the least interactions with other medications and are the best tolerated) or an SNRI (desvenlafaxine, duloxetine or venlafaxine); start low, increase slowly to avoid side effects, which may be more prominent in the medically ill*
Is there fatigue?	Consider using a more stimulating antidepressant (e.g. reboxetine, an SSRI or moclobemide)*
Are there melancholic features?	Use a broad-spectrum antidepressant (e.g. mirtazapine starting at 15 mg, or nortriptyline starting at 10 to 20 mg); an antipsychotic may also be required Patients with little or partial response may require augmentation with mood stabilisers and other medications or ECT, in consultation with a psychiatrist*
Is there significant anxiety or insomnia?	Use a more sedating antidepressant: mirtazapine 15 mg can be helpful for both anxiety and insomnia Bupropion and some TCAs (e.g. small doses of nortriptyline, doxepin) may assist with substance withdrawal*
Is there significant pain?	Consider treating pain with CBT, mindfulness, physical measures (such as massage and stretching) Some antidepressants (e.g. TCAs and mirtazapine) potentiate analgesics; of the TCAs, amitriptyline is particularly useful for pain and depression, while others (e.g. nortriptyline) may have less anticholinergic side effects
Is the patient on other medications for medical illnesses?	Consider using an SSRI (sertraline, citalopram, escitalopram) or mirtazapine, which have the least interactions with other medications; consider on a case by case basis*
<small>ABBREVIATIONS: CBT = cognitive behavioural therapy; ECT = electroconvulsive therapy; SSRI = selective serotonin reuptake inhibitor; SNRI = serotonin and noradrenaline reuptake inhibitor; TCA = tricyclic antidepressant. * TRADE NAMES: amitriptyline – Endepr; bupropion – Clorprax, Prexaton, Zyban SR; citalopram – Celapram, Celica, Ciazil, Cipramil, Citalobell, Talam, Talohexal; desvenlafaxine – Pristiq; doxepin – Deptran, Sinequan; duloxetine – Cymbalta; escitalopram – Esipram, Lexapro; mirtazapine – Avanza, Avanza Softab, Axit, Mirtazon, Remeron; moclobemide – Amira, Aurorix, Clobemix, Maosig, Mohexal; nortriptyline – Allegron; reboxetine – Edronax; sertraline – Concorz, Eleva, Sertra, Setrona, Xydep, Zoloft; venlafaxine – Eflexor-XR.</small>	

often manifest as regrets, complaints, guilt and unresolved relationship difficulties. Dealing with 'unfinished business' is especially important in the context of a fatal disease.

Panic symptoms are common in patients with conditions such as asthma, chronic obstructive pulmonary disease, cardiac failure, severe pain and medical obesity. Some patients with these conditions may have a previous anxiety disorder that can worsen, with fears of possible death and disability due to their medical condition. Others may develop an anxiety problem as their medical condition worsens. Clinical psychologists can assist through cognitive behavioural therapy (CBT) techniques.

Appropriate use of exercise is extremely beneficial in its own right in most medical illnesses, even advanced heart failure. Aerobic exercise and weights training have antidepressant properties and also provide a feeling of empowerment and increase mobility and physical stability, as well as providing a greater sense of wellbeing, accomplishment and social support. Exercise can be prescribed; occupational therapists and physiotherapists can be helpful here. Information sheets on the prescribing of and benefits of exercise are available on the Black Dog Institute website (see the box on this page).

Stress management and relaxation techniques will assist with pain, sleep and apprehension and should improve relationships. Early techniques for stress management featured the 'power of positive thinking', and early relaxation techniques often involved progressive muscle relaxation with attention to breathing, such as Jacobsen's progressive relaxation, which was first described in the late 1930s. It is now recognised that there is a myriad of techniques to suit different personality types and coping styles. Some people encounter problems with 'letting go' and can become panicky when they try to relax. This needs to be discussed and a different type of relaxation technique

Website resources for GPs and patients

Beyondblue

Downloadable fact sheets and resources for health professionals are available from: http://www.beyondblue.org.au/index.aspx?link_id=7.102

Downloadable information resources for patients are available from: http://www.beyondblue.org.au/index.aspx?link_id=7.980

- Resources relating to depression and chronic physical illness include fact sheets on coronary artery disease, after stroke, dementia, arthritis, asthma, Parkinson's disease, breast cancer and prostate cancer
- Resources relating to recovery from depression include fact sheets on reducing stress, sleeping well, keeping active, changing your thinking – cognitive behavioural therapy, reducing alcohol and other drugs (including smoking), other treatments for depression and anxiety, recovery, and healthy eating for people with depression, anxiety and related disorders

Resources mentioned in article

- **Anxiety disorders.** Fact sheet 21 and information card. Available at: http://www.beyondblue.org.au/index.aspx?link_id=7.980
- **Antidepressant medication. Advice for adults.** Fact sheet 11. Available at: http://www.beyondblue.org.au/index.aspx?link_id=7.980
- **SPHERE Questionnaire.** http://www.beyondblue.org.au/index.aspx?link_id=89.677

Black Dog Institute

Downloadable information sheets, fact sheets and other resources for health professionals and patients are available from: <http://www.blackdoginstitute.org.au/healthprofessionals/resources/overview.cfm>

Resources mentioned in article

- **About melancholic depression.** Depression information for GPs. Available at: <http://www.blackdoginstitute.org.au/docs/3.AboutMelancholicDepression.pdf>
- **An integrative depression model and Understanding your depressive episode.** An assessment and management tool, including a sheet for patients and doctors to work on together. Available at: http://www.blackdoginstitute.org.au/docs/UnderstandingYourDepressiveEpisode_000.pdf
- **A rational model for antidepressant drug prescription.** Available at: http://www.blackdoginstitute.org.au/docs/arationalmodelforantidepressantdrugprescription_000.pdf
- **Exercise and depression.** Fact sheet. Available at: <http://www.blackdoginstitute.org.au/docs/ExerciseandDepression.pdf>
- **Mindfulness in everyday life.** Patient handout. Available at: <http://www.blackdoginstitute.org.au/docs/10.MindfulnessinEverydayLife.pdf>
- **Quick relaxation techniques.** Patient handout. Available at: <http://www.blackdoginstitute.org.au/docs/17.RelaxationSheetQuickRelaxationTechniques.pdf>
- **Relapse signature: learning from experience.** Patient handout. Available at: <http://www.blackdoginstitute.org.au/docs/18.RelapseSignatureLearningfromExperience.pdf>
- **'Use it or lose it' – the benefits of exercise.** Patient handout. Available at: <http://www.blackdoginstitute.org.au/docs/6.ExerciseUseitofLoseit.pdf>

National Prescribing Service: Therapeutic Advice and Information Service

Drug information line for health professionals.

Telephone: 1300 138 677; online enquiry: http://www.nps.org.au/health_professionals/consult_a_drug_information_pharmacist/therapeutic_advice_and_information_service

considered. The trick is to match the type of relaxation exercises to the patient. An information sheet acting as a sampler of different techniques, so that patients can see what sort of exercise suits them, is available on the Black Dog Institute website (see page 43). Information sheets and material about anxiety and panic are also available on the beyondblue website (see page 43).

Physiotherapy can play an important part in the nonpharmacological treatment of depression. Many relaxation exercises emphasise breath control, which may be unhelpful when dyspnoea is part of the medical problem. Physiotherapists can assist with information about correct breathing posture, combined with appropriate relaxation strategies that do not focus on breathing.

CBT techniques can increase a patient's sense of mastery (promoting a sense of control), aid symptoms such as pain, insomnia and anxiety, and help prevent depression relapse.² Mindfulness is a form of self-awareness training adapted from mindfulness meditation. It has been described as a state of being in the present, accepting things for what they are. It was originally developed to assist with mood regulation in relation to pain and chronic illness and has been found to have considerable health benefits. An information sheet on mindfulness is available on the Black Dog Institute website (see page 43).

The experience of keeping a personal journal of their experience¹⁰ and other creative techniques (such as art and poetry) can allow patients to express their emotions and help them make sense of the meaning to them of their illness.

Depression with medical comorbidity can challenge patients' coping styles. It is worth eliciting what works for them normally and during a crisis ('what's the biggest crisis you have had prior to your illness, and how did you deal with it?').

Many illnesses will raise issues of mortality and other spiritual and existential issues. It is important to ask whether the

patient wants to talk about this and/or needs assistance from pastoral care or other spiritual/religious counsellors.

Pharmacological management

Feelings of depression and hopelessness can lead to the development of high blood pressure. Patients who feel depressed or hopeless have higher rates of cardiac arrhythmias and sudden cardiac death because of higher circulating levels of cortisol and noradrenaline, and also changes in heart rate variability and platelet aggregation. It is important to reassure and empower patients as much as possible and to treat depression prior to surgical interventions.

Dual action antidepressants – that is, the serotonin and noradrenaline reuptake inhibitors (SNRIs; desvenlafaxine [Pristiq], duloxetine [Cymbalta], venlafaxine [Efexor-XR]) – can improve depression, insomnia and pain tolerance simultaneously. For people with depression who are medically ill, compared with in otherwise well patients, it is even more important to start antidepressants at low doses and increase doses slowly because these patients are particularly prone to nausea, agitation and drug interactions. Information sheets about antidepressant drugs are available on the Black Dog Institute and beyondblue websites (see page 43). It is helpful to select target symptoms and consider the side effect profiles of medications. Medications should then be given for a trial period to address these goals, and stopped if they are not beneficial. It is wise to discuss the prescribing of antidepressants with the pharmacist and the patient's medical team. Advice about specific drug interactions can be sought from the National Prescribing Service's Therapeutic Advice and Information Service (see the box on page 43).

Pain, insomnia, multiple medications and interventions can all act to precipitate and prolong depression, and all are compounded where there is substance abuse involving prescribed and nonprescribed medications. It is important that treatment

addresses all of these factors.

There is a complicated relation between substance use and mental illness, in that although people often start using substances in times of depression or stress, the substances themselves and the evolution of medical illnesses can lead to more mood disorders. Agents such as bupropion (Clorprax, Prexaton, Zyban SR) and nortriptyline (Allegron) are both antidepressant and anticraving, and other antidepressants can assist with mood maintenance after withdrawal. There are now several newer medications for use in drug dependence, such as varenicline (Champix) and buprenorphine (Subutex), and these make it possible for people to cease substance use relatively comfortably. The dosages of other medications need to be reviewed as plasma levels may change after smoking cessation; this can provide an incentive for smoking cessation.

Reappraisal further down the track

Some problems only become overt as time goes on. This can occur where there are developing illnesses, complications or emerging medical psychological issues. If the problems persist, it is important to take a fresh look and/or get a second opinion. Substance abuse issues also often only surface later.

On recovery from the depressive episode, it is important to 'have another look' at the patient to reassess any biological or personality vulnerability that can be improved to reduce the risk of relapse or recurrence. A resource for health professionals and an accompanying patient information sheet about understanding depression is available on the Black Dog Institute website (see page 43). This patient information sheet provides a framework for understanding what factors are important in the onset and course of depressive episodes for specific individuals. It is intended to be used collaboratively by individuals and their GPs

to promote understanding of the depressive episodes and where treatment should be directed during the episode and what needs to be done to prevent recurrence.

There is also a patient handout about the concept of a 'relapse signature' on the Black Dog Institute website (see page 43). This resource provides information on learning from what happened in an episode of depression and how to 'get in early' and prepare for any further depressive episodes.

Conclusion

Depression in the context of medical illness is often viewed as being 'understandable' and not requiring treatment. The term 'depression' is used in a range of conditions, including normal experience ('I'm depressed'...), personality traits (pessimism, self-criticism, worrying and tendency to 'stress') and adjustment reactions/disorders (including grief) as well as clinical disorders (major melancholic and nonmelancholic depressions). Differing approaches are required to treat the depression and enhance the patient's ability to cope with the medical illness and other comorbidities. In those patients with multiple medical, psychiatric and substance use comorbidities, ceasing substance use can assist mental as well as physical health. MT

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COMPETING INTERESTS: Professor Wilhelm has written material for GP workshops on depression-related topics and also resources that appear on the Black Dog Institute website.

Online CPD Journal Program

List three pointers to clinical depression in a person with a medical illness.

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