

4 Managing depression in a community setting

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There are a range of effective treatments for depression that general practitioners can consider

At least 15% of the population will suffer from significant depression at some stage of life, and at any one time about 3%–5% will have significant symptoms. In general practice, 5% of patients have major depression and another 5% have a less severe form of this illness. The depression seen in general practice often coexists with physical disorder, or may present with physical rather than psychological complaints.

The disability caused by depression has been underestimated by the medical profession; it has a pervasive effect on physical function, bodily pain, general health, family, work and social relationships, as well as mental health.

The nature of depression in general practice

Depressed patients experience more impairment in quality of life than patients with common medical disorders.¹ They are also higher consumers of general health care.² This stems from greater use of general medical services rather than higher mental health treatment costs (US\$2390 per year as against US\$1397 for patients with common medical disorders).³

General practice patients with depression usually have shorter episodes of depression and meet fewer diagnostic criteria for major depression than those seen in psychiatric clinics.⁴ Severity is the best predictor of the persistence of depressive symptoms (the more severe the depression, the more likely it is to persist).^{5,6}

Tricyclic antidepressants (TCAs) are the most commonly prescribed antidepressant in general practice, and are usually prescribed at too low a dose:⁷ 80%–90% of prescriptions are less than 125–150 mg daily,⁸ below recommended guidelines for management of depression in general practice.⁹ In one study, 52% of the general practitioners used lower than recommended daily treatment doses (as against 17% of psychiatrists) and 40% of the general practitioners as against 7% of psychiatrists prescribed for less than the recommended minimum continuation period.¹⁰

Are treatments for depression effective in the community setting?

Most studies have been undertaken in psychiatric outpatient practice, with findings being extrapolated to general practice.

Antidepressant medications

There is no doubt about the effectiveness of antidepressants in outpatient psychiatric practice. A comprehensive meta-analysis of both inpatient and outpatient controlled trials has demonstrated response



A black, leafless tree with broken branches in bare surroundings is a metaphor for the depressed self. The tree is separated from another by a fence. The second tree has foliage developing, signifying a recovery from depression. Reproduced with permission from the Cunningham Dax Collection of Psychiatric Art in the Mental Health Research Institute of Victoria.

Synopsis

Patients with depression may be hopeless of recovery, but effective treatments are available.

- The diagnosis of major depression indicates a strong likelihood of response to antidepressants and/or psychological treatment.
- Patients with moderate to severe major depression benefit from antidepressant medications.
- Most patients do best with a combination of antidepressant medications and some form of psychological therapy.
- Psychological treatments alone are most useful with mild to moderate levels of depression.
- It is necessary to trial an antidepressant for at least four to six weeks before changing to a different treatment.
- Patients who respond to acute treatment should have that continued for at least four to nine months at the same dose.
- Long-term treatment should be considered for those with recurrent depression, particularly if it is severe.

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rates of 50% to 55%, compared with a 30% response rate to placebo treatment.¹¹

A trial of amitriptyline¹² in general practice found it superior to placebo in patients with major depression, but not in those with minor levels of depression. This study was important in demonstrating that TCAs are of benefit in relatively mild levels of depression, but not in the mildest range. Patients with Hamilton Depression Rating Scale scores of 12 or less were just as likely to respond to the placebo treatment. (The clinician-rated Hamilton scale¹³ is a widely accepted index of the severity of depression. Scores of 17 or more indicate a significant degree of depression; 7–12 indicates mild depression; and less than 7 is within the normal population range.)

Psychological treatments

The major study of psychological treatments in depression in general practice is that of Elkin et al., who compared imipramine plus good clinical care with cognitive therapy, interpersonal therapy and good clinical care plus placebo.¹⁴ In patients with Hamilton scores of less than 20 (moderately severe depression) there were no differences between any of these treatments, whereas in patients with more severe scores interpersonal therapy was more effective than placebo, although cognitive therapy was not. However, other studies have shown cognitive therapy to be more effective than placebo and of similar efficacy to antidepressants in outpatient depression.^{15,16} More recently, Mynors-Wallis et al. found that problem solving was as effective as amitriptyline, and more effective than placebo.¹⁷

Recommendations for treatment

The outcome of a consensus conference of members of the Royal College of General Practitioners and the Royal College of Psychiatrists was published in 1992,⁸ and a year later the Agency for Health Care Policy and Research (AHCPR) of the US Department of Health and Human Services published the *Clinical practice guideline on depression in primary care*.¹¹ Both guidelines are now regarded as important benchmarks, although there has been some criticism, particularly with

1 DSM-IV criteria for major depression

At least five of the following symptoms for at least two weeks (symptom 1 or 2 must be present):

1. Depressed mood
2. Loss of interest or pleasure
3. Significant appetite or weight loss or gain
4. Insomnia or hypersomnia
5. Psychomotor agitation or retardation
6. Fatigue or loss of energy
7. Feelings of worthlessness or excessive guilt
8. Impaired thinking or concentration; indecisiveness
9. Suicidal thoughts/thoughts of death.

DSM-IV = *Diagnostic and statistical manual of mental disorders*, 4th ed.²³

Case history 1: Depression presenting as anxiety and insomnia

A successful middle-aged businessman presented with a one-year history of marked anxiety and insomnia — symptoms quite out of character for him.

These appeared to have developed in the context of business difficulties out of his control. This had led to the necessity to lay off a large number of long-serving loyal staff, a task he found very difficult.

Closer questioning revealed that the insomnia and anxiety were manifestations of major depression. Whereas he usually thrived on work, he found himself reluctant to go to the office. He had also lost interest in his golf, and did not enjoy his holidays. He had become forgetful, for example paying for goods in a shop and then leaving without them. His concentration had become impaired, which made it difficult for him to read documents.

He had never been depressed previously. Apart from a benign enlarged prostate his physical health had been good. He did not abuse alcohol or other substances. There was no evidence of any marital or family problems.

In view of the disabling nature of his depression, he was prescribed a selective serotonin reuptake inhibitor (SSRI), with a marked improvement of his symptoms over the next month. As he recovered, his usual ability to deal with work pressures returned. However, his symptoms recurred when withdrawal of the SSRI was attempted nine months later, so he has continued drug treatment.

regard to their strong emphasis on antidepressant drugs and correspondingly less stress on the role of psychological treatments, particularly for the mildly depressed.^{18,19} The major Australian guidelines are in the *Psychotropic drug guidelines*.²⁰ Clinical practice guidelines for managing depression in young people have recently been published by the National Health and Medical Research Council.^{21,22}

Acute management of depression

Which forms of depression are likely to respond to treatment?

The diagnosis of major depression (Box 1) — with or without melancholic features — indicates a strong likelihood of response to antidepressants or psychological treatment. In less severe forms of depression, either long-lasting (dysthymic disorder) or more acute (adjustment disorder with depressed mood), response to treatment is less predictable. None the less, some patients with dysthymic disorder and adjustment disorder do respond to antidepressant therapies.

Most patients with major depression in general practice do not have melancholic or endogenous features (i.e., pervasive anhedonia, psychomotor retardation or agitation, or reduced emotional reactivity). Patients with bipolar disorder (manic-depressive illness) must be identified by questioning about possible past episodes of hypomania or mania, as such patients will require a mood stabiliser (e.g., lithium, carbamazepine or sodium valproate) in conjunction with the chosen antidepressant therapy. Similarly, patients with psychotic

depression (those with delusions and/or hallucinations) must be identified, as they will require treatment with electroconvulsive therapy (ECT) or a combination of antidepressants and antipsychotics.

Many depressed patients seen in general practice also have a physical disorder, and the depression is often caused by their disability, discomfort or distress. This does not preclude the effectiveness of medications or psychological treatments. Rarely, depression may be due directly to the physical condition (for example, with some endocrinopathies or cerebrovascular disease) or the drugs used to treat the disorder (e.g., corticosteroids or treatments for Parkinson's disease).

When should antidepressant medications be used?

Most patients with major depression — particularly those with moderate to severe levels, or melancholic features — will benefit from antidepressant medications. However, research such as that of Paykel et al.¹² indicates that antidepressants are more effective than placebo even in those with relatively mild depression.

Factors that may suggest the use of antidepressants include incomplete response to psychotherapy alone, a patient request for antidepressants, chronic symptoms (two years or more), previous episodes of depression, a family history of depression, and previous response to antidepressants.¹¹

Combined antidepressant medication and psychological treatments

Most patients do best with a combination of antidepressant medications and some form of psychological therapy. The need for combined medication and psychological treatments may be indicated by an incomplete response to antidepressants or psychological treatments alone or a poor recovery from symptoms between episodes of depression.

When to use psychological treatments alone

Such treatments are probably most useful for those with mild to moderate levels of depression. Other features that would suggest this choice of therapy include chronic psychosocial problems, a previous positive response to psychological treatments, failure to respond to antidepressant medications, and patient preference.

What is an adequate course of treatment?

Recommendations vary; for example, the AHCPR guidelines¹¹ recommend continuing medication for six weeks before considering another treatment. The study of Nierenberg et al. of response to treatment with fluoxetine found that 36% of patients with no improvement at two weeks finally responded to treatment at eight weeks.²⁴ The response rates at eight weeks in patients with no improvement at four and six weeks were 19% and 7%, respectively. In view of these results, a four- to six-week trial of an antidepressant is reasonable before trying a drug from another class.

Unfortunately, there are no studies to indicate how long a course of psychological treatment should be continued before such treatment is changed.

Continuation of therapy

Patients who respond to acute treatment should continue therapy with the same dose of antidepressant for four to nine months to prevent a relapse of the original episode.²⁵

Maintenance therapy

Studies have confirmed the value of ongoing medications in preventing recurrences of depression.²⁶ Maintenance therapy should be considered for those who have had three previous episodes of depression, those with two previous episodes if such episodes were recent and severe, and those with a family history of bipolar disorder or recurrent depression.¹¹ For such patients, treatment should be continued for at least two to five years and, for some, indefinitely.

When to refer

Referral to a psychiatrist should be considered when the patient has bipolar disorder, psychotic depression or active suicidal thoughts; when there is no response to one or two trials of treatment; or when there may be a need for ECT (ECT is effective for patients with psychotic depression or melancholic depression not responding to antidepressants). For patients requiring specialised psychological treatments, referral to either a psychiatrist or clinical psychologist may be necessary, the choice depending on factors such as individual therapist skill and the cost of therapy.

Case history 2: A professional woman with depression

A very capable professional woman in her mid-30s became depressed as a consequence of difficulties in conceiving a child. The couple had delayed trying to have children, and desperately desired to become parents. The difficulty in conceiving, and consequent involvement in an IVF program, also led to significant marital stress.

The patient had started to cry frequently and had some suicidal thoughts (although she had no intent to act upon them). She had little energy and was easily fatigued — in contrast to her usual active and productive self. She developed insomnia, her concentration was impaired, and she lost her appetite. At times she would shop and spend more than usual in order to cheer herself up.

She was referred to a counsellor for both individual and marital therapy. The individual counselling focused upon the issues of her grief over not being able to bear children, her guilt about not attempting to conceive earlier, and the tension within the marriage. However, despite skilled therapy for an adequate time, her symptoms persisted.

At that point she was referred for a trial of antidepressants. To the surprise of her medical practitioner, she responded rapidly to a selective serotonin reuptake inhibitor. A few months later, when she decided to stop taking the drug, the symptoms returned, again remitting on reintroduction of the antidepressant. Her symptomatic improvement then allowed her to engage more productively in psychotherapy, but she has also elected to continue antidepressant drug therapy.

2 Antidepressants marketed in Australia since 1990 — dosage and adverse effects

Drug	Dose (mg)			Adverse effects
	Start	Usual	Maximum	
Selective serotonin reuptake inhibitors (SSRIs)				
Fluoxetine	20	20–40	80	Nausea, anorexia, weight loss, diarrhoea
Paroxetine	20	20–40	50	Insomnia, somnolence
Sertraline	50	50–100	200	Agitation, restlessness, anxiety
Fluvoxamine	100	100–200	300	Tremor, sweating
Citalopram	20	20–40	60	SIADH
Reversible selective monoamine oxidase inhibitor (RIMA)				
Moclobemide	300	300–600	600	Prolonged bleeding time
Serotonin–noradrenaline reuptake inhibitor (SNRI)				
Venlafaxine	75	75–150	375	Nausea, vomiting
5-HT₂ antagonist/serotonin reuptake inhibitor				
Nefazodone	100	200–400	600	Dizziness
Adverse effects for SSRIs, RIMA, and SNRI				
Headache				
Insomnia				
Tremor				
Nausea, anorexia, constipation				
Dizziness				
Dry mouth				
Insomnia, somnolence				
Sweating				
Asthenia				
Hypertension (at doses \geq 225 mg)				
Abnormal ejaculation				
Adverse effects for 5-HT₂ antagonist/serotonin reuptake inhibitor				
Dry mouth				
Nausea				
Somnolence				
Dizziness				
Constipation				
Asthenia				
Lightheadedness				
Blurred vision				

SIADH = syndrome of inappropriate antidiuretic hormone secretion.

Antidepressants

TCAs are still the most commonly prescribed antidepressants in many countries, including Australia. Although there has been concern that the newer antidepressants may be less effective than TCAs in severe or melancholic depression,²⁷ the vast majority of depressed patients seen in the general practice setting have mild to moderate depression, for which the new antidepressants are as effective as the old. As there is consistent evidence of underprescription of TCAs and as the new medications are safer in overdose, the following order of antidepressant use in general practice is recommended:

First line: Selective serotonin reuptake inhibitors (SSRIs), venlafaxine, nefazodone, moclobemide or mianserin.

Second line: TCAs (desipramine or nortriptyline are preferred as they have fewer anticholinergic effects and are less sedating).

Third line: Irreversible monoamine oxidase inhibitors (MAOIs).

Details of the dosage, side effects and interactions of the more recently introduced antidepressants are provided in Boxes 2 and 3.

What should be done if the patient doesn't respond to a first-line antidepressant after four to six weeks?

At present there are few scientific data upon which to answer this question. While the occasional patient may benefit from switching within a particular class of medications (e.g., the

SSRIs), there is more likelihood of response in changing to a different class (e.g., from an SSRI to a TCA or venlafaxine). An alternative approach is to augment the antidepressant with lithium, liothyronine sodium or pindolol (the latter for SSRIs only). (The pharmacological mechanisms of lithium and liothyronine augmentation are uncertain, but pindolol is thought to act by blocking the inhibitory 5-HT_{1a} receptors on the serotonergic neuronal cell bodies — an action that would enhance serotonergic transmission.)

What should be done if the patient cannot tolerate the adverse effects of an antidepressant?

First, it should be emphasised that many adverse effects of the antidepressants (e.g., nausea with SSRIs or sedation with TCAs) do settle within the first one or two weeks of treatment. If adverse effects are severe and persistent, it is best to switch classes of antidepressants, as classes such as SSRIs share adverse effect profiles. There is some evidence to suggest that patients may tolerate one drug in a class while failing to tolerate another (e.g., Brown et al.²⁸ found that most patients who could not tolerate fluoxetine were able to tolerate sertraline).

Guidelines for changing antidepressants are provided in the *Psychotropic drug guidelines*.²⁰ The major safety issues are (1) avoiding the serotonergic syndrome by allowing adequate time for drug clearance when switching between the irreversible MAOIs and other antidepressants, and (2) allowing adequate time for drug clearance when switching between SSRIs and other antidepressants, as SSRIs inhibit negative cytochrome

P450 enzymes responsible for the metabolism of many of the antidepressants.

Withdrawal from antidepressants

Similar withdrawal syndromes have been described with the TCAs, SSRIs and venlafaxine, usually in patients who have been taking antidepressants for at least several months or at a high dose. The clinical syndrome is characterised by abdominal pain or discomfort, nausea, vomiting, diarrhoea, insomnia, rhinorrhoea, light-headedness and flu-like symptoms. Such withdrawal symptoms, while discomforting, are not dangerous and last only a maximum of two weeks.

Psychological treatments

A number of psychological treatments have been shown to be effective for depressed psychiatric outpatients (cognitive therapy and interpersonal therapy in particular; Box 4), but such treatments do not easily translate to general practice.

It is useful to discuss psychological treatments in terms of non-specific and specific forms:

Non-specific psychological treatments

These techniques were well described in the UK consensus statement on the management of depression in general practice.⁸ They may involve:

- support, understanding, encouragement and explanation
- meeting with other members of the family, or friends

- advising environmental change
- recommending self-help groups
- contacting governmental and other agencies (e.g., housing departments) on behalf of the patient
- helping the patient with problem solving
- discussing chronic social difficulties with the patient.

Specific psychological treatments

Cognitive therapy and interpersonal therapy have been shown to be effective in depression, although most studies have been undertaken in the psychiatric setting. Some small studies, such as that of Scott et al.,²⁹ have attempted (with some success) to tailor cognitive therapy to a form suitable for the general practitioner. There is also a trend in Australia for general practitioners to be trained in cognitive therapy skills. (One example of this is the Master in Psychological Medicine program for general practitioners offered through the University of New South Wales.)

The study of Mynors-Wallis et al. found that problem solving undertaken in either the patient's home or a local health centre was as effective as amitriptyline and more effective than placebo.¹⁷ Two of the three therapists in that study were general practitioners. Patients were given the rationale that emotional problems are caused by problems in the circumstances of their life, and that if problems were dealt with effectively symptoms would improve. Problems were then identified, listed, and dealt with one-by-one using problem

3 New antidepressants — important interactions

Drug	Other medication	Clinical features of interaction	Comments
SSRIs	1. Irreversible MAOIs; moclobemide	Serotonergic syndrome — hypomania, confusion, myoclonus, hypertension, tremor, diarrhoea, death	Do not prescribe SSRIs within two weeks of MAOIs. Do not prescribe MAOIs within five weeks of fluoxetine, two weeks of other SSRIs
	2. Medications metabolised by cytochrome P450 enzymes in liver (e.g., TCAs, antipsychotics, some antiarrhythmics)	SSRIs inhibit metabolism, leading to increased levels in blood	Avoid TCA/SSRI combination. May need to prescribe lower doses of other medications with SSRIs
Moclobemide	1. Pethidine	Uncertain — but life-threatening interaction with irreversible MAOIs	Avoid combination
	2. SSRIs, TCAs	Serotonergic syndrome deaths reported with overdose — particularly with clomipramine	Avoid combination with TCAs, SSRIs, even at therapeutic doses (particularly clomipramine)
Venlafaxine	Irreversible MAOIs; moclobemide	Serotonergic syndrome (as above)	Do not prescribe venlafaxine within two weeks of MAOIs. Do not prescribe MAOIs within one week of venlafaxine
Nefazodone	1. Irreversible MAOIs; moclobemide	Serotonergic syndrome	Do not prescribe nefazodone within two weeks of MAOIs. Do not prescribe MAOIs within one week of nefazodone
	2. Terfenadine, astemizole and cisapride	Nefazodone inhibits metabolism, leading to potentially toxic levels in blood, producing serious cardiac events, including death	Combinations contraindicated

MAOI = monoamine oxidase inhibitor; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant.

4 Psychological therapies

Cognitive-behavioural therapy

The principle of cognitive-behavioural therapy is that irrational beliefs and distorted attitudes towards the self, the environment and the future perpetuate depressed mood. Treatment aims to help patients become aware of these beliefs, and so become more able to realistically appraise themselves and their life experiences.

Case example

A 50-year-old doctor presented with a five-year history of depression precipitated by work and financial difficulties. Assessment of his premorbid personality style revealed marked perfectionist traits and very high self-expectations. He viewed minor failings as a severe indictment of his capacities and self-worth. Treatment of his depression therefore incorporated both antidepressants (to treat the symptoms) and cognitive-behavioural therapy (to help him recognise his damaging thought patterns and modify them to interpret his own behaviour and experiences more realistically).

Interpersonal therapy

Interpersonal therapy seeks to identify interpersonal losses, role disputes and transitions, social isolation, or deficits in social skills that may lead to depression. It works on the principle that losses must be mourned, role disputes and transitions must be recognised and resolved, and that deficits in social skills must be overcome to permit the acquisition of social supports.²⁸

Case example

A middle-aged businessman presented with depression occurring in the context of difficulties in a work partnership. On further questioning it became apparent that he had always had difficulties with asserting himself appropriately and could not cope with conflict or anger. He was a quiet person who preferred to please others, "bottling up" his feelings rather than dealing openly with disagreements. His treatment program therefore included assertiveness and social skills training, in addition to marital therapy and antidepressants.

Problem solving

The principle underlying problem solving is that depression is caused by problems in life circumstances, and that if problems are dealt with symptoms may improve. Problems are identified, listed and dealt with one-by-one.

Case example

A teacher in his forties presented with persistent low-grade depression despite a number of adequate courses of antidepressants. After taking the patient's history, it was clear that he was a markedly obsessional person who was highly distressed by his work with developmentally disabled pupils. An excellent teacher, he would set high standards for himself, and had difficulty coping with the behavioural disturbance of some of the pupils. After discussion, he recognised that his work context was a significant contributor to his depression and decided to leave face-to-face teaching. He took up a position coordinating correspondence courses, which resulted in a marked resolution in his levels of stress and depression.

solving methods. The first session took 60 minutes, with five subsequent sessions of 30 minutes.

Conclusion

Much of the depression seen in the community can be dealt with adequately by general practitioners, who have a wide range of antidepressant medications and psychological treatments at their disposal to alleviate suffering from this severe and disabling disorder.

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