**Depression**

[Authored by Dr Laurence Knott, 21 Mar 2014](https://patient.info/doctor/depression-pro)

**PATIENT PROFESSIONAL REFERENCE**

Professional Reference articles are written by UK doctors and are based on research evidence, UK and European Guidelines. They are designed for health professionals to use. You may find the [**Seasonal Affective Disorder**](https://patient.info/health/seasonal-affective-disorder-leaflet) article more useful, or one of our other [**health articles**](https://patient.info/health).

**IN THIS ARTICLE**

* [Classification](https://patient.info/doctor/depression-pro#nav-0)
* [Epidemiology](https://patient.info/doctor/depression-pro#nav-1)
* [Presentation](https://patient.info/doctor/depression-pro#nav-2)
* [Differential diagnosis](https://patient.info/doctor/depression-pro#nav-3)
* [Associated diseases](https://patient.info/doctor/depression-pro#nav-4)
* [Investigations](https://patient.info/doctor/depression-pro#nav-5)
* [Management](https://patient.info/doctor/depression-pro#nav-6)
* [Complications](https://patient.info/doctor/depression-pro#nav-7)
* [**Prognosis**](https://patient.info/doctor/depression-pro#nav-8)

Depression refers to both negative affect (low mood) and/or absence of positive affect (loss of interest and pleasure in most activities) and is usually accompanied by an assortment of emotional, cognitive, physical and behavioural symptoms.

It is the most common psychiatric disorder and carries a high burden in terms of treatment costs, effect on families and carers and loss of workplace productivity. It is currently ranked the third most prevalent moderate and severe disabling condition globally by the World Health Organization (WHO)[[1](https://patient.info/doctor/depression-pro#ref-1)]. It may become a chronic disorder with ongoing disability, particularly if inadequately treated. More than 80% of patients with depression are managed and treated in primary care, with those seen in secondary care being skewed towards much more severe disease[[2](https://patient.info/doctor/depression-pro#ref-2)].

**Classification**

Current National Institute for Health and Care Excellence (NICE) guidance uses the Diagnostic and Statistical Manual Fourth Edition (DSM-IV) classification[[3](https://patient.info/doctor/depression-pro#ref-3)]. To diagnose major depression, this requires at least one of the core symptoms:

* Persistent sadness or low mood nearly every day.
* Loss of interests or pleasure in most activities.

Plus some of the following symptoms:

* Fatigue or loss of energy.
* Worthlessness, excessive or inappropriate guilt.
* Recurrent thoughts of death, suicidal thoughts, or actual suicide attempts.
* Diminished ability to think/concentrate or increased indecision.
* Psychomotor agitation or retardation.
* Insomnia/hypersomnia.
* Changes in appetite and/or weight loss.

Symptoms should have been present persistently for at least two weeks and must have caused clinically significant distress and impairment. They should not be due to a physical/organic factor (eg, substance abuse) or illness (although illness and depression commonly co-exist). Severity is based on the extent of symptoms and their functional impact:

* **Subthreshold depressive symptoms** - <5 symptoms.
* **Mild depression** - few, if any, symptoms in excess of the 5 required to make the diagnosis, with symptoms resulting only in minor functional impairment.
* **Moderate depression** - symptoms or functional impairment are between 'mild' and 'severe'.
* **Severe depression** - most symptoms present and the symptoms markedly interfere with normal function. It can occur with or without psychotic symptoms.

Normal sadness exists along a continuum from clinically significant depression: differentiation is based on the severity, persistence and the degree of functional impairment and disability associated with the low mood.

**DSM-5**

DSM-5 was published in 2013. It proposes the following changes to the classification of depressive disorders[[4](https://patient.info/doctor/depression-pro#ref-4)]:

* Persistent depressive disorder - this term is proposed to encompass both chronic major depressive disorder and dysthymia.
* Removal of the major depression bereavement exclusion - the diagnosis of major depression was excluded in people who had recently been bereaved. This has been removed, leaving more leeway for clinical judgement.
* A new category of mixed anxiety/depressive disorder.

**Epidemiology**

* Data from 298 UK general practices showed that the incidence of diagnosed depression fell from 22.5 to 14.0 per 1,000 person-years at risk from 1996 to 2006. The incidence of depressive symptoms, however, rose threefold from 5.1 to 15.5 per 1,000 person-years at risk. The total incidence adding these two incidences together remained unchanged, suggesting that there was a trend for GPs to document symptoms rather than formal diagnoses. There was an association with deprived areas[[5](https://patient.info/doctor/depression-pro#ref-5)].
* Annually, 5% of adults have an episode of depression. About one in four women and one in ten men will develop depression severe enough to require treatment at some time in their lives. Most depressive states are at the mild-to-moderate end of the spectrum and it is these that are mainly seen in primary care[[6](https://patient.info/doctor/depression-pro#ref-6)].
* Chronic physical illness increases the risk of depression. NICE issued specific guidance regarding depression in adults with a chronic physical health problem[[7](https://patient.info/doctor/depression-pro#ref-7)].

**Risk factors**

* Female sex - in almost all studies, women have a higher prevalence, incidence and morbidity associated with depressive disorders compared with men. The gender difference is likely to be due to a complex interaction between biological, psychological and sociocultural vulnerabilities[[8](https://patient.info/doctor/depression-pro#ref-8)]. There is an increased incidence of depression during pregnancy and in the postnatal period - see separate articles [Depression in Pregnancy](https://patient.info/doctor/depression-in-pregnancy) and [Postnatal Depression](https://patient.info/doctor/postnatal-depression-pro).
* Past history of depression.
* Significant physical illnesses causing disability or pain.
* Other mental health problems, such as dementia.
* Depression is much more common in people from the African-Caribbean, Asian, refugee and asylum seeker communities[[9](https://patient.info/doctor/depression-pro#ref-9)].

**Presentation**[[3](https://patient.info/doctor/depression-pro#ref-3)]

**Screening**

This is covered by a separate article on recognition of depression: [Screening for Depression in Primary Care](https://patient.info/doctor/screening-for-depression-in-primary-care).

Depression is common but is often undetected by the medical profession - only about half of individuals with major depression are identified by their GP. However, a diagnosis of depression in primary care has a sensitivity of about 50% and specificity of 81%, with the risk of misidentification outweighing the risk of missed cases[[10](https://patient.info/doctor/depression-pro#ref-10)]. In other words, GPs may be good at ruling out those without depression but may need to consider more cautiously cases where depression might be present.

Somatisation is the most important cause of missed diagnosis but about two thirds of depressed patients present with somatic symptoms, making it critical always to consider emotional health in a differential[[2](https://patient.info/doctor/depression-pro#ref-2)]. Many patients seen have a pre-existing physical illness which can also divert attention away from their mental state. In the elderly, depression can present as pseudodementia, with abnormalities of memory and behaviour that are typical of true dementia.

The NICE guidelines encourage a case-finding approach with at-risk groups (individuals with a past history of depression or a chronic health problem with associated functional impairment) using a two question approach:

* During the past month, have you:
  + Felt low, depressed or hopeless?
  + Had little interest or pleasure in doing things?

Where there is an affirmative answer to either question, further evaluation should be triggered. **NB**: negative response does not exclude depression.

**Assessment**[[6](https://patient.info/doctor/depression-pro#ref-6)]

Self-report symptom scales are widely used and include:

* The [Patient Health Questionnaire (PHQ-9)](https://patient.info/doctor/patient-health-questionnaire-phq-9)
* The Hospital Anxiety and Depression (HAD) Scale[[11](https://patient.info/doctor/depression-pro#ref-11)]
* Beck's Depression Inventory

Whilst these can be helpful in staging depression, *do not rely on a symptom count alone* to make a diagnosis of depression.

An individual considered likely to have depression should be fully assessed, including:

* Full history and examination, including mental state examination, enquiring directly about suicidal ideas, delusions and hallucinations. Consider organic causes of depression such as hypothyroidism or drug side-effect. Establish the duration of the episode.
* Review of related functional, interpersonal and social difficulties. Involve family members or carers, with the patient's consent, to obtain third-party history if appropriate. Note whether there is evidence of self-neglect, psychosis or severe agitation. Consider cultural factors.
* Past psychiatric history, including previous episodes of depression or mood elevation, response to previous treatment and comorbid mental health conditions.
* Patient safety and risk to others - suicidal intent should be assessed regularly.

Depression should be assessed as mild, moderate or severe depending on the extent and impact of symptoms and level of functional impairment and/or disability and this will determine what level of treatment to initiate[[3](https://patient.info/doctor/depression-pro#ref-3)].

**Differential diagnosis**

* [Bipolar disorder](https://patient.info/doctor/bipolar-disorder-pro).
* [Schizophrenia](https://patient.info/doctor/schizophrenia-pro) (depression may co-exist).
* [Dementia](https://patient.info/doctor/dementia-pro) may occasionally present as depression and vice versa.
* [Seasonal affective disorder](https://patient.info/doctor/seasonal-affective-disorder-pro).
* Bereavement: depressive symptoms begin within 2-3 weeks of a death (uncomplicated bereavement and major depression share many symptoms but active suicidal thoughts, psychotic symptoms and profound guilt are rare with uncomplicated bereavement).
* Organic cause - eg, [hypothyroidism](https://patient.info/doctor/hypothyroidism).
* Drug adverse effects are an uncommon cause of depression. Medications that may cause depressed mood include:
  + Centrally acting antihypertensives (eg, methyldopa).
  + Lipid-soluble beta-blockers (eg, propranolol).
  + Benzodiazepines or other central nervous system depressants.
  + Progesterone contraceptives, especially medroxyprogesterone injection.

**Associated diseases**

* Dysthymia (recently classified by DSM-5 as a subtype of persistent depressive disorder) is a chronic depressive state of more than two years in duration, which does not meet full criteria for major depression and is not the consequence of a partially resolved major depression. People with dysthymia are likely to experience episodes of major depression. Dysthymia increases with age.
* Eating disorders: [anorexia nervosa](https://patient.info/doctor/anorexia-nervosa-pro) and [bulimia nervosa](https://patient.info/doctor/bulimia-nervosa-pro).
* [Substance misuse](https://patient.info/search.asp?searchterm=SUBSTANCE+ABUSE&collections=PPsearch) is frequently associated with depression.
* Other psychiatric conditions may co-exist with depression (eg, [generalised anxiety disorder](https://patient.info/doctor/generalised-anxiety-disorder-pro), [panic disorder](https://patient.info/doctor/panic-disorder), [obsessive-compulsive disorder](https://patient.info/doctor/obsessive-compulsive-disorder-pro), [personality disorders](https://patient.info/doctor/personality-disorders-and-psychopathy)).
* Some medical conditions have known associations with depression:
  + [Parkinson's disease](https://patient.info/doctor/parkinsonism-and-parkinsons-disease).
  + Chronic diseases such as [diabetes](https://patient.info/search.asp?searchterm=DIABETES+MELLITUS&collections=PPsearch) and [cardiac disease](https://patient.info/search.asp?searchterm=cardiac%2520disease&collections=PPsearch).
  + [Cerebrovascular disease](https://patient.info/search.asp?searchterm=Cerebrovascular%2520disease&collections=PPsearch).
  + Endocrine disorders such as [hyperthyroidism](https://patient.info/doctor/hyperthyroidism), [Cushing's syndrome](https://patient.info/doctor/cushings-syndrome-pro), [Addison's disease](https://patient.info/doctor/adrenal-insufficiency-and-addisons-disease) and [hyperparathyroidism](https://patient.info/doctor/hyperparathyroidism-pro).
  + Cancer, especially [pancreatic](https://patient.info/search.asp?searchterm=pancreatic%2520cancer&collections=PPsearch).
  + Autoimmune conditions.

**Investigations**[[6](https://patient.info/doctor/depression-pro#ref-6)]

Investigations are used to exclude organic causes for depression; they are not mandatory and should be used according to clinical judgement.

* Blood tests may include blood glucose, U&Es, LFTs, TFTs, calcium levels, FBC and inflammatory markers.
* Other tests may include magnesium levels, HIV or syphilis serology, or drug screening.
* Imaging (MRI or CT brain scanning) may be indicated where presentation or examination is atypical or where there are features suspicious of an intracranial lesion (eg, unexplained headache or personality change). Seek specialist advice.

**Management**

Doctors and patients can use Decision Aids together to help choose the best course of action to take[[12](https://patient.info/doctor/depression-pro#ref-12)].

Traditionally, primary care management of depression has been concentrated on the use of antidepressants. There is now evidence supporting the efficacy of non-drug alternatives but these have frequently not been available[[13](https://patient.info/doctor/depression-pro#ref-13),[14](https://patient.info/doctor/depression-pro#ref-14)]. The Government has targeted additional money in order to develop new local services, known as 'Improving Access to Psychological Therapies' (IAPT), the impact of which is beginning to take effect[[15](https://patient.info/doctor/depression-pro#ref-15)].

NICE published an evidence update in June 2013 on depression in children and young people which states that factors such as a history of physical abuse or parental marital discord may influence response to treatment[[16](https://patient.info/doctor/depression-pro#ref-16)].

Following is a brief summary of the stepped management proposed by NICE guidance[[3](https://patient.info/doctor/depression-pro#ref-3)]:

**Treatment of mild-to-moderate depression**

* Consider watchful waiting, assessing again normally within two weeks.
* Consider offering one or more low-intensity psychosocial interventions, guided by patient preference:
  + Guided self-help based on [cognitive behavioural therapy (CBT)](https://patient.info/doctor/cognitive-and-behavioural-therapies) principles - book prescription schemes, or internet resources. There is some evidence that after three months of individual CBT, group CBT can be equally effective[[17](https://patient.info/doctor/depression-pro#ref-17)].
  + Evidence suggests that group CBT delivered at school may not reduce symptoms in young people at high risk of depression and may increase the reporting of symptoms[[16](https://patient.info/doctor/depression-pro#ref-16)].
  + Computerised CBT[[18](https://patient.info/doctor/depression-pro#ref-18)].
  + Relaxation therapy - more effective than no, or minimal, treatment[[19](https://patient.info/doctor/depression-pro#ref-19)].
  + Brief psychological interventions (6-8 sessions) including problem-solving therapy, brief CBT and counselling.

Antidepressants are *not* recommended for the initial treatment of mild depression, because the risk:benefit ratio is poor. However, their use may be considered:

* If mild depression persists after other interventions, or is associated with psychosocial and medical problems.
* In mild depression complicating the care of physical health problems.
* When a patient with a history of moderate or severe depression presents with mild depression.
* With subthreshold depressive symptoms present for at least two years or persisting after other interventions.

**Treatment of moderate-to-severe depression**

* Offer antidepressant medication *combined with* high-intensity psychological treatment (CBT or interpersonal therapy (IPT)). For an individual with a chronic health problem and moderate depression, this should be high-intensity psychological treatment *alone* in the first instance[[7](https://patient.info/doctor/depression-pro#ref-7)].
* In young people, combining CBT and newer antidepressants may be better in the short term than either therapy alone, particularly with regard to global functioning[[16](https://patient.info/doctor/depression-pro#ref-16)].
* Make an urgent psychiatric referral if the patient has active suicidal ideas or plans, is putting themself or others at immediate risk of harm, is psychotic, severely agitated or is self-neglecting. The use of the [Mental Health Act](https://patient.info/doctor/compulsory-hospitalisation) may be necessary in some instances.
* [Electroconvulsive therapy (ECT)](https://patient.info/doctor/electroconvulsive-therapy) may be used to gain fast and short-term improvement of severe symptoms after all other treatment options have failed, or when the situation is thought to be life-threatening[[20](https://patient.info/doctor/depression-pro#ref-20)].

The advice about exercise as a treatment is conflicting. In addition to the above treatments, the NICE guideline advises regular exercise as a possible treatment. A Cochrane review published in 2012 supports this advice, concluding that exercise seems to improve depressive symptoms[[21](https://patient.info/doctor/depression-pro#ref-21)]. However, the Cochrane review ends by saying "caution is required in interpreting these results". In contrast, a large research trial published in 2012 found that the addition of an exercise programme to the usual care for depression did not improve the outcome of depression or reduce the use of antidepressants compared with usual care alone[[22](https://patient.info/doctor/depression-pro#ref-22),[23](https://patient.info/doctor/depression-pro#ref-23)].

**Drug treatment**

* **What sort of antidepressant?** Selective serotonin reuptake inhibitors (SSRIs) are used as first-line antidepressants in routine care because they are as effective as tricyclic antidepressants and less likely to be discontinued because of side-effects; also because they are less toxic in overdose[[3](https://patient.info/doctor/depression-pro#ref-3)].
* Recent meta-analyses have concluded that SSRIs have benefit in severely depressed patients[[24](https://patient.info/doctor/depression-pro#ref-24)]. However, evidence for their efficacy in mild-to-moderate depression above placebo effects is much less clear[[25](https://patient.info/doctor/depression-pro#ref-25)]. An American review of six studies suggested that antidepressants were effective in non-severe major depression[[26](https://patient.info/doctor/depression-pro#ref-26)].
* **Which SSRI?**:
  + Guidance suggests that we choose a generic SSRI (eg, citalopram, fluoxetine, paroxetine, or sertraline) when treating an individual with antidepressants for the first time, with the assumption that they have equivalent efficacy[[6](https://patient.info/doctor/depression-pro#ref-6),[27](https://patient.info/doctor/depression-pro#ref-27)].
  + However, a recent meta-analysis suggested that escitalopram had the highest probability of remission and is the most effective and cost-effective pharmacological treatment in a primary care setting[[28](https://patient.info/doctor/depression-pro#ref-28)].
  + Fluoxetine is the antidepressant of choice for children and young people. It is the only antidepressant licensed for this use. The evidence base concerning the use of other antidepressants in this age range is limited[[16](https://patient.info/doctor/depression-pro#ref-16)].
  + Where a patient has concurrent physical health problems, citalopram or sertraline may be preferred, as they have less risk of significant drug interactions[[6](https://patient.info/doctor/depression-pro#ref-6)].
  + Where a patient has previously been treated for depression, be guided by past patterns of response/non-response to antidepressants.
  + Treatments such as dosulepin, phenelzine, combined antidepressants and lithium augmentation of antidepressants should be initiated only by specialist mental healthcare professionals.
  + St John's wort should not be recommended because of uncertainty about appropriate doses, variation in the nature of preparations and potential serious interactions with other drugs.
* Prior to initiating any medication, discuss the patient's fears of addiction or other concerns about medication; over a quarter of patients newly prescribed an antidepressant by their GP never obtain their prescription or take more than a single dose[[29](https://patient.info/doctor/depression-pro#ref-29)]. Warn about expected side-effects and discontinuation reactions.
* Inform patients about the delay in onset of effect, the time course of treatment and the need to take medication as prescribed. Make available written information appropriate to the patient's needs.

**Clinical Editor's notes (August 2017)**  
Dr Hayley Willacy recommends this recent meta-analysis of antidepressant (AD) use and the risk of incident diabetes[[30](https://patient.info/doctor/depression-pro#ref-30)]. The results showed a significant association between AD use and risk for diabetes (Pooled relative risk [RR], 1.27; P<.001). When the analysis was restricted to only six high-quality studies, the association became stronger (RR, 1.40; 95% CI, 1.24-1.57). The exact pathophysiological reason behind this association is not yet known but several possible theories have been suggested: some antidepressants may worsen glucose metabolism through weight gain; some research has suggested that depression can directly increase the risk for diabetes; other researchers have suggested a reverse causation effect, ie diabetes triggers the risk for depression, leading to prescription of antidepressants.

**Monitoring**[[6](https://patient.info/doctor/depression-pro#ref-6)]

* See patients, who are not considered to be at increased risk of suicide, two weeks after starting treatment and continue to review regularly as appropriate.
* Monitor for signs of akathisia, suicidal ideas and increased anxiety and agitation, particularly in the early stages of treatment with an SSRI.
* See patients, who are considered to be at increased risk of suicide or who are younger than 30 years old, one week after starting treatment. Regularly review (every 2-4 weeks) in the first three months or until the risk is no longer significant. Where there is a high risk of suicide, prescribe a limited quantity of antidepressants and consider additional support such as more frequent contacts with primary care staff, or telephone contacts.

Where there is partial or no response to medication at 2-4 weeks:

* Check adherence to and side-effects from the treatment.
* Consider increasing the dose of the antidepressant.
* Consider switching to an alternative antidepressant - either another SSRI, mirtazapine, moclobemide, reboxetine, venlafaxine or a tricyclic. Always check guidance regarding switching and the need for 'wash out times' and careful dosage adjustment. Avoid tricyclic antidepressants or venlafaxine when there is a risk of overdose.
* Duloxetine is licensed for major depressive disorder.
* Flupentixol is listed in the British National Formulary (BNF) for the treatment of depression but not commented on in any detail in the NICE guidelines[[31](https://patient.info/doctor/depression-pro#ref-31)].
* Agomelatine was not licensed at the time of the publication of the NICE guidelines but is listed in the BNF as a melatonin receptor agonist and a selective serotonin-receptor antagonist[[31](https://patient.info/doctor/depression-pro#ref-31)].

Treatment duration:

* For patients who have benefited from the use of an antidepressant, they should be continued for at least six months after remission to reduce the risk of relapse.
* Patients who have had two or more depressive episodes in the recent past and who have experienced significant functional impairment during the episodes, should be advised to continue antidepressants for two years. A much longer duration of treatment may be required for some patients.
* Patients who are considered to be at substantial risk of relapse or who have residual symptoms, should be considered for referral for either individual CBT or mindfulness-based cognitive therapy.

When stopping antidepressants:

* Reduce doses gradually over a four-week period; some people may require longer periods and fluoxetine can usually be stopped over a shorter period.
* For mild discontinuation/withdrawal symptoms, reassure the patient and monitor symptoms. For severe symptoms, consider re-introducing the original antidepressant at the effective dose (or another antidepressant with a longer half-life from the same class) and reduce gradually while monitoring symptoms.

**Referral**  
In addition to the urgent referral necessary when an individual is actively suicidal, referral to secondary care may be necessary where there is[[6](https://patient.info/doctor/depression-pro#ref-6)]:

* Uncertain diagnosis, including possible bipolar disorder.
* Failed response to two or more interventions.
* Recurrence of depression <1 year from previous episode.
* More persistent suicidal thoughts.
* Comorbid substance, physical, or sexual abuse.
* Severe psychosocial problems.
* Rapid deterioration.
* Cognitive impairment.

**Complications**

* Depression is a major cause of impaired quality of life and reduced productivity. Social difficulties are common (eg, social stigma, loss of employment, marital break-up). Associated problems, such as anxiety symptoms and substance misuse, may cause further disability.
* Depression is also associated with increased mortality: more than half of all individuals who take their own life have evidence of major depressive illness. Depressed men are at higher risk than women are of suicide, particularly in combination with alcohol misuse and impulsive or aggressive personality traits[[32](https://patient.info/doctor/depression-pro#ref-32)].
* A history of attempted suicide.
* High levels of hopelessness.
* High ratings of suicidal tendencies.
* Depression increases the risk of developing and dying from coronary heart disease[[33](https://patient.info/doctor/depression-pro#ref-33)].

**Prognosis**

The outlook varies with the severity of the condition:

* The average length of an episode of depression is 6-8 months and, with mild depression, spontaneous recovery is likely[[6](https://patient.info/doctor/depression-pro#ref-6)].
* For major depression, approximately 80% of people who have received psychiatric care for an episode will have at least one more episode in their lifetime, with a median of four episodes.
* The outcome for those seen in primary care also seems to be poor, with only about a third remaining well over 11 years and about 20% having a chronic course[[34](https://patient.info/doctor/depression-pro#ref-34)]. In light of this, some argue for a model of chronic disease management for depression, akin to that for diabetes or asthma[[35](https://patient.info/doctor/depression-pro#ref-35)].
* There is inadequate evidence to determine the clinical effectiveness or cost-effectiveness of low-intensity interventions for the prevention of relapse or recurrence of depression[[36](https://patient.info/doctor/depression-pro#ref-36)].
* Risk factors for increased risk of depression recurrence include[[2](https://patient.info/doctor/depression-pro#ref-2)]:
  + ≥3 episodes of major depression.
  + High prior frequency of recurrence.
  + An episode in the previous 12 months.
  + Residual symptoms during continuation treatment.
  + Severe episodes - eg, 'suicidality', psychotic features.
  + Long previous episodes.
  + Relapse after drug discontinuation.
  + One study found that people reporting poor or fair self-rated health had a worse prognosis with respect to long-term depression than those reporting good or excellent health[[37](https://patient.info/doctor/depression-pro#ref-37)].