Unipolar depressive disorders

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Abstract

Depression is a common relapsing mood disorder that causes significant distress and impairment in social and occupational functioning. It is associated with an increased risk of death, not only through suicide, but also from physical illnesses such as cardiovascular disease. It is under-recognized and undertreated and should be considered in individuals at high risk of depression, for example those suffering from chronic physical health problems. Its aetiology is multifactorial, and co-morbidity with other psychiatric disorders is common. Assessment of depression requires an assessment of the duration, symptom severity, suicide risk and functional impairment of the current episode, co-morbid diagnoses, past mood and treatment history, and developmental, social and family history. Treatment is guided by illness severity, presentation and prior history. It includes psychosocial interventions, medications and their combination, with antidepressant medication reserved for persistent and moderate to severe depression. Prevention of relapse is a priority; risk factors for this should be assessed and used to guide the choice of prophylactic drug and psychological treatment.

Keywords Aetiology; antidepressants; assessment; cognitive behaviour therapy; diagnosis; dysthymia; major depression; psychotherapy; selective serotonin reuptake inhibitors (SSRIs); treatment

Key points

- Depression is frequently undiagnosed and undertreated; consider depression in hight-risk groups, including those with a chronic physical illness
- Assessment must include determination of suicide risk, any history of elevated mood and current alcohol or substance misuse
- Psychosocial approaches should be used first in patients with mild depression
- Specific psychological treatments (e.g. cognitive behaviour therapy) and antidepressants are alternatives for moderate and more severe depression
- Selective serotonin reuptake inhibitors are first-line antidepressants
- Over-the-counter complementary and herbal treatments (e.g. St John's wort) are commonly used and can interact with prescribed medication
- Treated patients should be assessed regularly for symptom severity, suicidality and adverse effects, at least every 2 weeks initially but more often in those with higher suicide risk
- Antidepressant drug treatment trials should usually last 6–8 weeks before deciding insufficient efficacy, although a dose increase or change of treatment is indicated if there is no improvement after 4 weeks
- Use a symptom rating scale such as the Patient Health Questionnaire-9 or Hospital Anxiety and Depression Scale to aid assessment of severity and monitor treatment progress
- Combined drug and psychosocial treatment should be used in patients not responding to either alone
- Combination drug treatments are useful when there has been partial response to the first drug or a failure to respond to a number of trials
- Relapse prevention is a priority following successful treatment including continuing antidepressant drugs for at least 6–9 months at the full treatment dosage
- Patients at risk of recurrent episodes should be offered prophylactic (maintenance) medication or psychological treatment to prevent recurrence

How common?

'Clinical' depression (major depression in the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5); Table 1) has a point prevalence of 4.4%, with chronic subthreshold depression (dysthymia) adding an additional 2%.[1,2] Unipolar depressive disorders rank ninth in the world, and third in Europe, among causes of health-related disability, making up 2.8% and 3.8%, respectively, of the total disease burden.

Definition

Depression is a heterogenous syndrome consisting of core symptoms of pervasive low mood and/or lack of enjoyment

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(anhedonia) together with other emotional, cognitive and physical symptoms resulting in significant functional impairment (Table 1). Unipolar depression (considered here) occurs in the absence of a history of mood elevation (see *Bipolar disorder*, pp 661–663 of this issue); however, the boundary between unipolar depression and bipolar disorder is blurred and controversial.

Epidemiology

Onset is usually in the mid-20s but can occur at any time. The point prevalence of major depression rises steeply during adolescence, peaks at about 7.5% in the 40s with a slight decline into old age.[1] It is nearly twice as common in women than men across the age range, with higher rates associated with social disadvantage.[3] Depression is commonly associated with other psychiatric disorders, especially anxiety and substance-use disorders, and chronic physical illness;[2,4] for example, the incidence is increased two- to threefold in diabetes mellitus, coronary artery disease, end-stage renal failure and chronic obstructive pulmonary disease.

Pathology and pathogenesis

In the 'biopsychosocial' model of depression, developmental vulnerability caused by biological, psychological and social factors interacts with environmental precipitating and maintaining factors. 'Secondary' depression (symptomatically arising directly from a physical illness or treatment) can be difficult to separate from depression triggered by the physical condition.

Vulnerability to depression is hereditable, involving multiple genes interacting with developmental and environmental factors.[5] The monoamine theory postulates a functional decrease in serotonin (5-hydroxytryptamine) and/or noradrenaline (norepinephrine) neurotransmission leading to depression, which can be reversed by antidepressant drug treatment. However, many other neurochemical and neuroendocrine systems are implicated, including the hypothalamic–pituitary–adrenal axis and proinflammatory cytokines, as well as altered neurogenesis and synaptic plasticity. Reductions in grey matter volume, most consistently in the hippocampus, may reverse with recovery, but persistence has been reported in long-standing, recurrent depression. Functionally, there is altered processing of emotion-related stimuli and of the activity and connectivity of mood-related brain areas such as the amygdala and anterior cingulate cortex.[5] Vulnerability is strongly associated with childhood neglect or sexual abuse, personality factors (neuroticism), chronic social difficulties and isolation. Adverse life events

Abridged criteria for major depression and persistent depression/dysthymia

DSM-5 (American Psychiatric Association)

Major depressive disorder

Over the previous 2 weeks, five or more of the following have been present most of the time (must include at least one of the first two 'core' symptoms):

- depressed mood most of the day (e.g. sad, empty, hopeless)
- loss of interest or pleasure in almost all activities nearly every day
- significant appetite/weight loss or gain
- insomnia or hypersomnia
- psychomotor agitation or retardation (observable by others)
- fatigue or loss of energy
- feelings of worthlessness or excessive guilt
- diminished concentration or indecisiveness
- recurrent thoughts of death, or suicidal thoughts, plans or attempts

The symptoms cause clinically significant distress or impairment in functioning, and are not caused by a medical/organic factor or illness.

Severity: mild (few symptoms beyond minimum, mild functional impairment), moderate (symptoms and functional impairment between mild and severe), severe (most symptoms present, marked or greater functional impairment).

Classified as single episode or recurrent (at least one previous episode).

Persistent depressive disorder (includes dysthymia)

Depressed mood for most of the day, for more days than not, for at least 2 years, together with two or more of:

- poor appetite or overeating
- insomnia or hypersomnia
- low energy or fatigue
- low self-esteem
- impaired concentration or indecisiveness
- hopelessness

Must not have been symptom free longer than 2 months.

Note: the requirement not to meet criteria for major depression, found in previous editions, has been removed.

ICD-10 (World Health Organization)

Depressive episode – broadly similar to DSM-5, but two out of three 'typical' symptoms (depressed mood, decreased interest/enjoyment, fatiguability) are needed, and mild depression requires four, rather than five, symptoms.

Dysthymia – similar to DSM-5 persistent depressive disorder except must not meet the criteria for a depressive episode.

Table 1