Unipolar depression in adults: Clinical features

AUTHOR: Jeffrey M Lyness, MD
SECTION EDITOR: Peter P Roy-Byrne, MD
DEPUTY EDITORS: Sara Swenson, MD, David Solomon, MD

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: **Oct 2023.**
This topic last updated: **Oct 19, 2023.**

INTRODUCTION

Depression occurs along a continuum of severity, and depressive syndromes such as unipolar major depression are heterogeneous [1]. The multiple presentations of major depression stem in part from the several subtypes that have been identified and the many comorbid disorders that frequently occur.

This topic reviews the clinical features of depression in adults. The assessment, diagnosis, epidemiology, neurobiology, treatment, and prognosis of depression in adults are discussed separately, as are the clinical features and diagnosis of depression in pediatric and older adult patients:

- (See "Unipolar depression in adults: Assessment and diagnosis".)
- (See "Unipolar depression in adults: Epidemiology".)
- (See "Unipolar major depression in adults: Choosing initial treatment".)
- (See "Unipolar depression in adults: Choosing treatment for resistant depression".)
- (See "Pediatric unipolar depression: Epidemiology, clinical features, assessment, and diagnosis".)
- (See "Diagnosis and management of late-life unipolar depression".)

DEFINITIONS OF DEPRESSION

It is important to recognize the potential for confusion engendered by multiple uses of the term "depression." Depression may refer to a:

- Mood state, which may be normal or part of a psychopathological syndrome
- Syndrome, which is a constellation of symptoms and signs (eg, major depression or minor depression)
- Mental disorder that identifies a distinct clinical condition (eg, unipolar major depression)

As an example, major depression is a syndrome that occurs as a consequence of several disorders, including unipolar major depression (also called "major depressive disorder"), bipolar disorder, schizophrenia, substance/medication-induced depressive disorder, and depressive disorder due to another (general) medical condition [2].

SYMPTOMS

- **Depressed mood** – Depressed mood (dysphoria) is an essential feature of unipolar major depression (major depressive disorder) and persistent depressive disorder (dysthymia) [2]. Dysphoria can take many forms, such as feeling sad, hopeless, discouraged, "blue," or "down in the dumps." Patients who appear sad (eg, tearful) may initially deny sadness and state that they feel anxious, "blah," or have no feelings. In addition, increased and persistent annoyance, frustration, irritability, anger, or hostility occurs in roughly 50 percent of patients with major depression [3-5].

- **Loss of interest or pleasure** – Loss of interest or pleasure (anhedonia) in formerly pleasurable activities is also a cardinal symptom of unipolar major depression [2]. Patients experience events, hobbies, and activities as less interesting or fun, and may report that "they don't care anymore." Patients may withdraw from or lose interest in friends, and libido or interest in sex may decrease as well.

- **Change in appetite or weight** – Appetite and weight may decrease or increase in unipolar major depression, persistent depressive disorder, and premenstrual dysphoric disorder [2]. Some patients have to force themselves to eat, whereas others eat more and may crave specific foods (eg, junk food and carbohydrates).

- **Sleep disturbance** – Sleep disturbance frequently occurs in unipolar major depression, and can also occur in persistent depressive disorder and premenstrual dysphoric disorder

[2]. Problems with sleep manifest as insomnia or hypersomnia:

- Initial insomnia – Difficulty getting to sleep
- Middle insomnia – Waking in the middle of the night, with difficulty returning to sleep
- Terminal insomnia – Waking earlier than usual and remaining awake
- Hypersomnia – Prolonged nighttime sleep, or daytime sleeping

Many depressed patients describe their sleep as nonrestorative and report difficulty getting out of bed in the morning.

- **Fatigue or loss of energy** – Lack of energy (anergia) is described as feeling tired, exhausted, and listless. Patients may feel the need to rest during the day, experience heaviness in their limbs, or feel like it is hard to initiate or complete activities.

- **Neurocognitive dysfunction** – Unipolar major depression, persistent depressive disorder, and premenstrual dysphoric disorder can manifest with impaired ability to think, concentrate, or make decisions [2,6]. Patients may also appear easily distracted or complain of memory difficulties.

  For most depressed patients (especially younger and middle-aged adults), cognitive symptoms are readily distinguished from those caused by delirium or dementia. Neurocognitive dysfunction in depression is generally mild and marked by subjective complaints more than objective findings on examination. In older adult patients, memory problems may be mistaken for those of a neurodegenerative dementia ("pseudodementia" or "dementia of depression"); these problems often abate with successful treatment of the depressive syndrome [2]. However, some patients with a neurodegenerative dementia initially present with an episode of major depression that includes memory difficulties.

  Based upon meta-analyses of neurocognitive studies that have compared patients with major depression with healthy controls, major depression is marked by deficits in [7-9]:

  - Attention.
  - Concentration.
  - Cognitive flexibility (concept or set shifting).
  - Executive function (eg, planning, problem solving, reasoning, and impulsivity).
  - Information processing (psychomotor) speed.

- Memory.
- Verbal fluency (listing as many words as possible from a category [eg, animals or fruits] in a set time, typically one minute).
- Social cognition (often referred to as "theory of mind"; the ability to infer the thoughts, intentions, or emotions of others based upon verbal and nonverbal communication such as facial expression, gestures, and body language).

Neurocognitive dysfunction is greater in patients who are less educated and older, and patients with more severe depressive symptoms [7]. In addition, cognitive impairments can interfere with occupational functioning [7] and persist after patients have remitted from major depression [8,10].

- **Psychomotor agitation or retardation** – Major depressive episodes may include psychomotor disturbances [2]:
  - Agitation – Excessive motor activity that is usually nonproductive, repetitious, and accompanied by a feeling of inner tension; examples include hand-wringing, pacing, and fidgeting.
  - Retardation – Generalized slowing of body movements, thinking, or speech. Speech volume, quantity, and inflection may be decreased, with increased latency in answering questions.

  Psychomotor disturbances are less common than other symptoms, but indicate that the patient is more severely ill [2,11].

- **Feelings of worthlessness or excessive guilt** – The self-perceptions of depressed patients may be marked by feelings of inadequacy, inferiority, failure, worthlessness, and inappropriate guilt [2]. Worthlessness and guilt can occur in unipolar major depression and persistent depressive disorder, and frequently manifest with misinterpreting neutral events or minor setbacks as evidence of personal failings.

- **Suicidal ideation and behavior** – Depressed patients can experience recurrent thoughts of death or suicide and may attempt suicide. Suicidal ideation may be passive, with thoughts that life is not worth living or that others would be better off if the patient was dead. By contrast, active suicidal ideation is marked by thoughts of wanting to die or commit suicide, and indicates the patient is severely ill. In addition, there may be suicide plans, preparatory acts (eg, selecting a time and location to commit suicide, purchasing a large amount of medication or a gun, or writing a suicide note), and suicide attempts.

Suicidality is increased by pervasive hopelessness (negative expectations for the future) and the conclusion that suicide is the only option to escape ceaseless and intense emotional pain. (See "Suicidal ideation and behavior in adults".)

Major depression with psychotic features may include auditory hallucinations telling (commanding) patients to commit suicide. (See "Unipolar major depression with psychotic features: Epidemiology, clinical features, assessment, and diagnosis", section on 'Psychotic features'.)

Depressed patients who intentionally commit acts of self-harm, such as superficially cutting or burning their skin, may state that their intent was to relieve pain and that they expected the injury to cause only mild to moderate harm [2]. Although patients may deny that they intended to kill themselves, this behavior (nonsuicidal self-injury) indicates the patient is severely depressed; nonsuicidal self-injury is associated with suicide attempts in which patients do intend to kill themselves [12].

Depression may be conceptualized as disturbances in:

- Emotions – Depressed mood and loss of interests or pleasure occur in depression. The nature of the "depressed" or dysphoric mood may vary. Some patients communicate intense sadness and emotional distress, while others report a sense of emotional numbness ("blahs") and exhibit a "flattened" affect on examination. The mood may be experienced subjectively by the patient or may be observable on mental status examination. Patients may present with prominent anxiety or irritability; although not specific for depression, these symptoms should be recognized as part of a depressive episode if they occur in the context and timeframe of other depressive features.

- Ideation or cognition – In addition to the cognitive symptoms listed in the Diagnostic and Statistical Manual, Fifth Edition, Text Revision (DSM-5-TR) (impaired concentration or memory, worthlessness or guilt, thoughts of death or suicide), other cognitive symptoms in depression include hopelessness, helplessness, and ruminative thinking (defined as the tendency to dwell on a single theme, which in depression tends to be negative).

- Neurovegetative (somatic) functioning – Somatic symptoms of depression include changes in sleep, appetite or weight, energy, libido, and psychomotor activity. Some symptoms, such as loss of energy or libido, occur in only one "direction" (decreased). Other symptoms, including changes in sleep, appetite or weight, and psychomotor functioning are potentially bidirectional; insomnia and anorexia with weight loss are most common in depression, but atypical features of hypersomnia or hyperphagia with weight gain can

occur. (See "Unipolar depression in adults: Assessment and diagnosis", section on 'Depressive episode subtypes (specifiers)'.)

Some studies suggest that the clinical presentation of major depression may vary between females and males, and that males may exhibit symptoms that are not included in the formal diagnostic criteria for major depression [13,14]. Depressed women may be more likely to report neurovegetative symptoms (eg, sleep, appetite, or energy problems) and other physical symptoms (eg, headaches, myalgias, or gastrointestinal symptoms), as well as emotional (eg, stress or crying easily) and psychosocial symptoms (eg, interpersonal difficulties) [15-18]. By contrast, it is hypothesized that depressed men present with symptoms that are "depressive equivalents," such as anger attacks/aggression (eg, suddenly losing control and hurting someone or threatening to hurt someone), substance use disorders, and risk-taking behavior (eg, casual or unsafe sex, or reckless driving) [17]. However, it is not clear that phenomena such as substance use disorders represent a symptom of depression or are better conceptualized as a separate or comorbid disorder.

In addition, depressive subtypes may vary between males and females, but the differences appear to be modest. An observational study (Sequenced Treatment Alternatives to Relieve Depression study) of 2541 outpatients with unipolar major depression found that major depression with anxious distress occurred in more women than men (48 versus 41 percent), as did major depression with atypical features (18 versus 13 percent) [18].

CARDINAL FEATURES

Heterogeneity of depression — Unipolar major depression is heterogeneous with regard to age of onset, symptom profile, subtypes, severity, and course of illness [1,19]. As an example, two patients can be diagnosed with major depression (table 1) without having even one symptom in common.

Continuum of severity — Depression occurs along a continuum that increases in severity from subsyndromal symptoms to the syndromes of minor depression, major depression, and persistent depressive disorder (dysthymia) [11,20-22]. As the number of symptoms increases, patients report greater severity (intensity) of depression, longer depressive episodes, and worse functioning.

A study of outpatients with either minor depression (n = 162) or major depression (n = 969) found that across all levels of severity (low, medium, and high) for each syndrome, certain

symptoms were present in approximately 60 percent or more of patients and were thus regarded as core symptoms of depressive syndromes [11]:

- Sad, irritable, or anxious mood
- Loss of interest or pleasure
- Impaired concentration and decision making
- Worthlessness and inappropriate guilt
- Hopelessness
- Fatigue or loss of energy

By contrast, the incidence of other symptoms was lower in less severely depressed patients and progressively increased as the level of depression severity increased, including sleep disturbance, change in appetite or weight, somatic complaints, and psychomotor agitation. Symptoms that occurred infrequently in minor depression but were highly prevalent in major depression included suicidal ideation and psychomotor slowing.

SUBTYPES OF DEPRESSIVE DISORDERS

Major depression and persistent depressive disorder are heterogeneous syndromes. The Diagnostic and Statistical Manual, Fifth Edition, Text Revision (DSM-5-TR) utilizes the following subtypes, which have been proposed in an attempt to provide greater diagnostic specificity [1,2,23]:

- Anxiety
- Atypical
- Catatonic
- Melancholic
- Mixed features
- Peripartum
- Psychotic
- Seasonal

However, these subtypes are not mutually exclusive, meaning that the same depressive episode may have features of more than one subtype. A study of anxious, atypical, and melancholic subtypes in patients with unipolar major depression (n >1000) found a pure form of one subtype in 39 percent, multiple subtypes in 36 percent, and no subtype in 25 percent [24].

The diagnosis of these subtypes is discussed separately. (See "Unipolar depression in adults: Assessment and diagnosis", section on 'Depressive episode subtypes (specifiers)'.)

Anxious — Unipolar major depression that includes high levels of anxiety symptoms is often called "anxious depression" [25]. These symptoms may take the form of worrying, rumination, health anxieties, and panic attacks. In addition, psychomotor agitation (eg, pacing and handwringing) may be considered an "anxiety equivalent." Anxiety symptoms that are part of a depressive syndrome may be difficult to distinguish from anxiety disorders that are comorbid with depressive disorders; these comorbid disorders are discussed separately. (See "Comorbid anxiety and depression in adults: Epidemiology, clinical manifestations, and diagnosis".)

In several studies that defined anxious depression as an episode of unipolar major depression that included high levels of anxiety, the anxiety component was derived from the Hamilton Rating Scale for Depression (table 2), with an anxiety/somatization subscale score ≥7 [26,27]. The subscale consisted of items 10 (psychic anxiety), 11 (somatic anxiety), 12 (gastrointestinal somatic symptoms), 13 (general somatic symptoms), 15 (hypochondriasis), and 17 (insight).

Anxiety may be a prodromal or residual feature of depressive episodes; as an example, postpartum depression often starts with increased anxiety [28]. In addition, anxiety may represent a response to functional impairment that is caused by the depressive syndrome.

Approximately 40 to 50 percent of major depressive episodes qualify as anxious depression [1,24,29]. Genetic, neuroimaging, and electroencephalography studies suggest that the neurobiology of anxious depression may differ from that of non-anxious depression [30,31].

The clinical utility of diagnosing major depression with anxious features is not clear. Some studies of acute unipolar major depression suggest that response to antidepressants is comparable in patients with or without the anxious subtype [24,29]. However, other studies suggest that antidepressants are less effective in patients with higher levels of baseline anxiety than patients with lower levels [26,32-34]. In addition, adjunctive anxiolytics can improve outcomes in anxious depression [32,35]. (See "Unipolar depression in adults: Treatment with anxiolytics".)

Atypical — Atypical depression is characterized by [2]:

- Reactivity to pleasurable stimuli (ie, feels better in response to positive events)
- Increased appetite or weight gain
- Hypersomnia
- Heavy or leaden feelings in limbs
- Longstanding pattern of interpersonal rejection sensitivity

According to DSM-5-TR, the core feature of atypical major depression is mood reactivity (ie, feeling better in response to positive events) [2]. However, this is not universally accepted, and

some studies indicate that the presence of hypersomnia or hyperphagia is sufficient for diagnosing atypical depression [1,23,36]. Historically, oversleeping and overeating were regarded as reversed or atypical symptoms of depression, in contrast to the "typical" depressive symptoms of insomnia and anorexia.

Atypical depression may account for 15 to 50 percent of depressive episodes [23,24,37,38], and may be associated with hypocortisolemia [23] and a history of trauma [39]. Compared with other types of depression, atypical depression is associated with female gender, earlier age of onset, family history of depression, higher rates of comorbidity (eg, anxiety disorders, substance use disorders, personality disorders, and obesity), more depressive symptoms, greater functional impairment, and more suicide attempts [1,36,40].

The clinical utility of diagnosing major depression with atypical features is not clear [41]. Although several studies of acute unipolar major depression suggest that response to antidepressants is comparable in patients with or without the atypical subtype [24,29,37], other studies suggest that antidepressants are less effective in patients with atypical features [38].

Catatonic — Catatonic features are characterized by prominent psychomotor disturbances that occur during most of the depressive episode. (See "Catatonia in adults: Epidemiology, clinical features, assessment, and diagnosis" and "Catatonia: Treatment and prognosis".)

Melancholic features — Melancholic features are characterized by [1,2,23,42]:

- Disturbed affect that is unresponsive to improved circumstances
- Anhedonia
- Psychomotor agitation or retardation
- Neurocognitive impairment
- Interrupted sleep
- Loss of appetite
- Diurnal variation (mood and energy worse in the morning)

Melancholic features are present in approximately 15 to 30 percent of major depressive episodes [24,38,43,44] and are more likely to be found in severely ill inpatients, including those who are psychotic [1,2,44]. The tendency for melancholic features to repeat across recurrent episodes of major depression is only modest [2]. Neurocognitive dysfunction may be worse in melancholic major depression than nonmelancholic major depression [45]. Putative biological correlates of melancholic features include hypercortisolemia and disturbances in sleep architecture (eg, reduced rapid eye movement latency and deep-sleep time) [1,23,42].

The treatment implications of melancholic features are not clear. Some studies of unipolar major depression suggest that response to acute treatment with antidepressants is comparable in patients with or without the melancholic subtype [24,43,44]. Other studies suggest that antidepressants are less effective in patients with melancholic features than patients without melancholic features [29,38], and yet other studies have found that melancholic features were associated with higher rates of remission [46]. Nevertheless, melancholic features generally require pharmacotherapy or electroconvulsive therapy because of their poor response to placebos and psychotherapies, and melancholic features may respond better to tricyclic antidepressants and electroconvulsive therapy than to selective serotonin reuptake inhibitors [1,23,42].

Mixed features — In DSM-5-TR, episodes of unipolar major depression (table 1) and persistent depressive disorder (dysthymia) (table 3) can each be accompanied by symptoms of the opposite polarity [2]. Unipolar major depression with mixed features is an episode that meets full criteria for major depression and includes at least three of the following manic/hypomanic symptoms:

- Elevated or expansive mood
- Grandiosity
- More talkative than usual
- Flight of ideas or racing thoughts
- Increased energy or goal-directed activity
- Decreased need for sleep
- Excessive involvement in pleasurable activities that have a high potential for painful consequences

Likewise, persistent depressive disorder with mixed features is an episode that meets full criteria for persistent depressive disorder and includes at least three of the manic/hypomanic symptoms. Some studies have also included irritable mood and psychomotor agitation as symptoms of mixed features [47,48].

Depressive disorders with mixed features represent a change from the previous edition of the Diagnostic and Statistical Manual (Fourth Edition, Text Revision; DSM-IV-TR) [49]. In DSM-IV-TR, mixed episodes were defined more narrowly, as periods lasting at least one week, during which full criteria were met for both a manic episode and a major depressive episode; these mixed episodes were classified as bipolar I mood episodes.

Major depression with mixed features appears to be common [50,51]. Prospective observational studies have found that among individuals with major depression (n = 488 and 573),

subthreshold hypomania was present in approximately 25 to 40 percent [47,52]. Comorbidity (eg, panic disorder and substance use disorders) and a family history of mania were more common in major depression with subthreshold hypomania, compared with major depression without hypomanic symptoms [47]. In addition, subthreshold hypomania was associated with eventually suffering an episode of mania or hypomania, and thus changing diagnosis from unipolar major depression to bipolar disorder.

Peripartum — Peripartum depression refers to unipolar major depression or persistent depressive disorder (dysthymia) that begins during pregnancy or within four weeks of childbirth [1,2,23]. (See "Unipolar major depression during pregnancy: Epidemiology, clinical features, assessment, and diagnosis" and "Postpartum unipolar major depression: Epidemiology, clinical features, assessment, and diagnosis".)

Psychotic — Episodes of major depression and persistent depressive disorder (dysthymia) may include psychotic features such as delusions and hallucinations [1,2,23]. (See "Unipolar major depression with psychotic features: Epidemiology, clinical features, assessment, and diagnosis".)

Seasonal — Seasonal affective disorder refers to recurrent mood episodes that regularly begin during a particular season (eg, winter) and remit during another season (eg, summer) [1,2,23]. (See "Seasonal affective disorder: Epidemiology, clinical features, assessment, and diagnosis".)

COMORBIDITY

Unipolar major depression is often concurrent with other psychiatric or general medical disorders. Many psychiatric and other medical conditions increase the risk of developing major depression [2].

Psychiatric — Most individuals with unipolar major depression have other psychiatric comorbidities, including anxiety and substance use disorders.

- **Prevalence of psychiatric comorbidities** – Reported prevalences of psychiatric comorbidities among individuals with major depression ranges from 69 to 76 percent [53,54]. Psychiatric comorbidities are also common among those with persistent depressive disorder (dysthymia) [55].
    - In a nationally representative survey in the United States, 76 percent of participants with a major depressive episode in the prior 12 months reported at least one comorbid

psychiatric disorder [53]. A study of 810 outpatients with major depression found comorbidity in 69 percent [54].

- Multiple comorbid psychiatric disorders can occur simultaneously in patients with major depression. Nationally representative surveys in 10 resource-rich countries found that among individuals with major depression in the prior 12 months, three or more comorbid disorders were present in 19 percent [56]. Another study of outpatients with major depression found a mean of 1.4 coexisting psychiatric diagnoses [54].

- **Types of comorbidities** – Psychiatric disorders that occur more commonly in individuals with depressive disorders include anxiety disorders (eg, generalized anxiety disorder, panic disorder, social anxiety disorder), alcohol and other substance use disorders, posttraumatic stress disorder, obsessive-compulsive disorder, attention deficit hyperactivity disorder, and personality disorders.

  In a nationally representative sample from the United States, adjusted odds ratios for comorbid psychiatric disorders among individuals with unipolar major depression ranged from two (for alcohol use disorder or specific phobia) to six (for generalized anxiety disorder) [57].

  Personality disorders are common psychiatric comorbidities, occurring in approximately 50 percent of individuals with depressive disorders. Common personality disorders in both unipolar major depression and persistent depressive disorder (dysthymia) are avoidant, borderline, dependent, and obsessive-compulsive personality disorders [58]. As an example, a large meta-analysis documented the presence of at least one personality disorder in 45 percent of those with major depression and 60 percent persistent depressive disorder [58]. Observational studies suggest that personality disorders can be diagnosed accurately during a depressive episode by rigorous application of diagnostic criteria [59,60]. The diagnosis of personality disorders is discussed separately. (See "Overview of personality disorders", section on 'Diagnosis'.)

- **Comorbidity generally precedes depression onset –** In most cases, onset of the comorbid psychiatric disorder precedes the onset of the depressive disorder.

  - A nationally representative survey in the United States found that among individuals with major depression and comorbidity (eg, anxiety disorders and substance use disorders), the onset of depression followed onset of the co-occurring disorder in nearly 90 percent [61].

- In a study of individuals with co-occurring persistent depressive disorder (dysthymia) and anxiety disorders, the anxiety disorders usually preceded onset of dysthymia [55].

- **Worse prognosis** – Any psychiatric comorbidity confers a worse prognosis for the depressive disorder than if the depression occurs in isolation [55,60,62].

Other medical illnesses — Other medical illnesses are common in individuals with depression, and their co-existence with depression worsens the prognosis for both depression and the medical condition.

- **Prevalence of medical comorbidities** – Depression and other medical illnesses often occur together. A substantial proportion of individuals with depression have multiple medical comorbidities [63], which are often more common in those with depression than in the general population [56]. Approximately 70 percent of individuals with depression have at least one other medical condition [56,63]. In one population-based study in multiple countries, 28 percent of individuals with major depression had three or more conditions [56].

- **Types of comorbidities** – Medical conditions seen in those with depression are not confined to specific types of disease or organ systems [64,65].

- **Directionality of relationship** – The directionality of the relationship between depression and medical comorbidities is not always clear (ie, whether depression increases the risk developing future medical disease or vice versa). For some diseases, the relationship seems bidirectional [66]. As an example, meta-analyses suggest that having depression is associated with a 32 percent increased risk of developing type 2 diabetes [67] and, conversely, that individuals with type 2 diabetes have a 24 percent increased relative risk of developing depression [68]. Similarly, a meta-analysis of 15 prospective observational studies (n >62,000 patients) found that depression at baseline increased the risk of subsequently becoming obese (odds ratio 1.6), and obesity at baseline increased the risk of depression at follow-up (odds ratio 1.6) [69].

  - **Effect of depression on medical comorbidities** – Compared with those without depression, individuals with depression are at increased risk of other medical illnesses [70-72]. A study comparing primary care patients with (n >140,000) and without depression (n >1,280,000) found that those with depression were more likely to have each of the 32 comorbid conditions that were assessed, including asthma, cancer, chronic kidney disease, coronary heart disease, diabetes, epilepsy, heart failure, hypertension, inflammatory arthritis, multiple sclerosis, pain, Parkinson disease, thyroid disorders, and viral hepatitis [63].

Depression also worsens the outcome of comorbid medical conditions, including the risk of death and hospitalization. As an example, depression in older patients with diabetes increased the relative risk for all-cause mortality by at least 36 percent over a two-year period [66,72-75]. Similarly, depression is associated with an increased risk of cardiovascular mortality, with more severe depression symptoms being associated with higher risk [76,77]. The relationship between depression and cardiovascular disease is discussed in detail separately (see "Psychosocial factors in acute coronary syndrome"). The presence of depression is also associated with an increased risk of hospitalization for other medical illnesses. In a prospective, multicohort study of 240,433 individuals, moderate to severe depression was associated with a 16 percent higher absolute risk of hospitalization over four years for 29 different medical illnesses, mainly endocrine, circulatory, and musculoskeletal diseases [66]. The excess risk of hospitalization for medical causes was greater than that for psychiatric and neurologic disorders combined (absolute risk increase of 1.7 percent).

- **Effect of medical comorbidities on depression** – Most chronic medical disorders, as well as many subacute and acute medical conditions and their treatments, increase the risk of subsequent depression [64]. The incidence of depression may be particularly high in neurologic (eg, Parkinson disease, stroke, and traumatic brain injury) [78-81], cardiovascular disorders [82,83], cancer [84], and conditions involving immune and inflammatory mechanisms (eg, systemic lupus erythematosus [85]).

  Although the presence of significant medical comorbidity worsens the prognosis of depression, treating depression in these patients is important and can improve self-rated health and functional status. (See "Unipolar depression in adult primary care patients and general medical illness: Evidence for the efficacy of initial treatments", section on 'Depression in general medical illness'.)

  Diagnosing major depression in the context of other medical disorders is discussed elsewhere. (See "Unipolar depression in adults: Assessment and diagnosis", section on 'General medical illness'.)

FUNCTIONAL IMPAIRMENT

Unipolar major depression was the second leading cause of disability in the world in 2010 and persistent depressive disorder (dysthymia) was the 19th leading cause [86]. Similarly, in the United States, major depression was the second leading cause of disability and dysthymia was the 20th [87]. Functional limitations associated with major depression in the United States are

comparable to or greater than the limitations associated with arthritis, cardiovascular disease, diabetes, and stroke [88]. In a nationally representative sample from the United States, functioning among those with severe major depression was approximately one standard deviation below the national mean [57].

Of the disability that was attributable to all mental and substance use disorders throughout the world in 2010, depressive disorders accounted for over 40 percent [89]. The burden of depressive disorders may be due in part to discrimination arising from stigma [90].

Psychosocial functioning in major depression is inversely proportionate to symptom severity [91], and most episodes are associated with poor psychosocial and physical functioning and poor self-rated health [61,92-94]. As an example, a nationally representative survey in the United States found that psychosocial functioning (work, household duties, relationships, and social roles) was severely or very severely impaired in almost 60 percent of individuals with major depression [61]. Patients with severe depression may become bed-bound and fail to perform basic activities of living including personal hygiene, toileting, and feeding.

The relationship between course of illness in patients with depression and functional impairment is discussed separately. (See "Unipolar depression in adults: Course of illness", section on 'Functioning'.)

Quality of life — Prospective studies have found that major depression is associated with reductions in quality of life, which refers to subjective satisfaction with one's physical, psychological, and social functioning (eg, satisfaction with work and relationships) [95]. The relationship between course of illness in patients with depression and quality of life is discussed separately. (See "Unipolar depression in adults: Course of illness", section on 'Quality of life'.)

SUICIDE

Many depressed patients kill themselves, and many more attempt to do so or otherwise inflict intentional self-injuries. (See "Unipolar depression in adults: Course of illness", section on 'Suicide' and "Suicidal ideation and behavior in adults", section on 'Psychiatric disorders'.)

VIOLENCE

Patients with depressive disorders may be more likely to perpetrate violence than the general population. In a national registry study with a mean follow-up of about three years, analyses that controlled for potential confounding factors (eg, age, sex, and comorbid substance use or

personality disorders) found that individuals diagnosed with depression were subsequently more likely to be convicted for violent crimes (eg, assault, robbery, or rape) compared with controls (odds ratio 2.6) [96]. The absolute risk of violent offending in men with and without depression was 3.7 and 1.2 percent, and among women with and without depression was 0.5 and 0.2 percent. However, it is not clear whether depression's association with violence is independent of clinically important unmeasured factors, such as personality trait vulnerabilities not captured in registry diagnoses of personality disorders.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Depressive disorders".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Depression in adults (The Basics)")
- Beyond the Basics topics (see "Patient education: Depression in adults (Beyond the Basics)" and "Patient education: Depression in children and adolescents (Beyond the Basics)")

SUMMARY

- Depression can refer to a mood state, syndrome, or specific mental disorder. (See 'Definitions of depression' above.)

- Depressive symptoms include depressed mood, loss of interest or pleasure, decreased appetite and weight or increased appetite and weight, insomnia or hypersomnia, fatigue, cognitive dysfunction, psychomotor agitation or retardation, feelings of worthlessness or guilt, and suicidal ideation and behavior. (See 'Symptoms' above.)

- Unipolar major depression is heterogeneous with regard to age of onset, symptom profile, subtypes, severity, and course of illness. (See 'Heterogeneity of depression' above.)

- Subtypes of depressive episodes include anxious, atypical, catatonic, melancholic, mixed features, peripartum, psychotic, and seasonal. (See 'Subtypes of depressive disorders' above.)

- Patients with unipolar major depression typically suffer comorbid psychiatric disorders, including anxiety disorders (agoraphobia without panic disorder, generalized anxiety disorder, panic disorder, separation anxiety disorder, social anxiety disorder, and specific phobia), posttraumatic stress disorder, obsessive-compulsive disorder, attention deficit hyperactivity disorder, oppositional defiant disorder, intermittent explosive disorder, and substance use disorders. Comorbid personality disorders are also common, especially avoidant, borderline, dependent, and obsessive-compulsive. (See 'Psychiatric' above.)

- Depression and comorbid general medical illnesses often occur together, and the relationship is bidirectional (depressed patients usually have at least one general medical condition, and patients with general medical disorders are often at increased risk of depression). General medical comorbidity is not specific to any disease type or organ system. (See 'Other medical illnesses' above.)

Topic 91774 Version 25.0