Bipolar disorder in adults: Clinical features

AUTHOR: Trisha Suppes, MD, PhD
SECTION EDITOR: Paul Keck, MD
DEPUTY EDITOR: 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: **Nov 28, 2022.**

INTRODUCTION

Bipolar disorder frequently disrupts mood, energy, activity, sleep, cognition, and behavior, as well as occupational and interpersonal functioning [1]. Out of 328 diseases that were studied worldwide in 2016, bipolar disorder was the 23rd leading cause of years lived with disability [2]. Pharmacotherapy within the context of a positive therapeutic alliance is central to managing morbidity and the risk of suicide. However, treatment following onset of the disorder is typically delayed for years [3].

This topic reviews the clinical features of bipolar disorder in adults. The assessment, diagnosis, and treatment of bipolar disorder in adults are discussed separately, as are the clinical features and diagnosis of bipolar disorder in children and adolescents, geriatric patients, and patients with rapid cycling (ie, four or more mood episodes in a 12-month period):

- (See "Bipolar disorder in adults: Assessment and diagnosis".)
- (See "Bipolar major depression in adults: Choosing treatment".)
- (See "Bipolar mania and hypomania in adults: Choosing pharmacotherapy".)
- (See "Bipolar disorder in adults: Choosing maintenance treatment".)
- (See "Pediatric bipolar disorder: Clinical manifestations and course of illness".)
- (See "Pediatric bipolar disorder: Assessment and diagnosis".)
- (See "Geriatric bipolar disorder: Epidemiology, clinical features, assessment, and diagnosis".)

- (See "Rapid cycling bipolar disorder: Epidemiology, pathogenesis, clinical features, and diagnosis".)

DEFINITION OF BIPOLAR DISORDER

According to the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR), and the World Health Organization's International Classification of Diseases 11th Revision (ICD-11), bipolar disorder is characterized by mood episodes that consist of mania (table 1), hypomania (table 2), and major depression (table 3) [1,4]. Mania and hypomania compose one pole of the disorder, and major depression the other pole.

The subtypes of bipolar disorder include bipolar I disorder and bipolar II disorder. Patients with bipolar I disorder experience manic episodes and nearly always experience major depressive and hypomanic episodes. Bipolar II disorder is marked by a history of at least one hypomanic episode, at least one major depressive episode, and the absence of manic episodes. The table (table 4) compares diagnostic features for the two subtypes. Additional information about diagnosing bipolar disorder is discussed separately. (See "Bipolar disorder in adults: Assessment and diagnosis".)

Although some studies have separately examined and compared the clinical features of bipolar I disorder and bipolar II disorder [5], most studies have combined the two subtypes.

CLINICAL PRESENTATION

Overview — Bipolar disorder can present with mania (table 1), hypomania (table 2), major depression (table 3), mixed features (mood episodes that are accompanied by concurrent symptoms of the opposite polarity), or psychotic features (eg, delusions or hallucinations) [1,6]. The severity of these syndromes varies widely across patients, as well as within an individual patient during the lifetime course of illness, and subsyndromal symptoms are common [7-9]. In addition, some symptomatic patients remit and become euthymic, while other patients transition immediately from one type of syndrome to another (eg, from major depression to mania) without an intervening period of euthymia [10].

The mood episode at onset of bipolar disorder is usually major depression [11]. In a study of 2308 patients, the first lifetime episode was [12]:

- Major depression in 54 percent

- Mania in 22 percent
- Mixed (concurrent symptoms of major depression and mania) in 24 percent

Prodrome — Many studies indicate that mood and nonmood prodromal signs and symptoms, such as irritability, anxiety, elevated mood, depressed mood, mood lability ("mood swings"), agitation, aggressiveness, disruptive behavior disorders (eg, conduct disorder), sleep disturbance, hyperactivity, and psychotic experiences (delusions or hallucinations) may precede onset of diagnosable bipolar disorder [13-18]. However, prodromal symptoms are nonspecific and their predictive value is uncertain. The same symptoms can occur during the prodrome of other psychiatric disorders, and the proportion of patients who experience a prodrome varies widely across studies.

Mania — Manic episodes (table 1) involve clinically significant changes in mood, energy, activity, behavior, sleep, and cognition (table 5) [1,6]. For any one patient, it is not known whether the symptom profile of mania is consistent across different episodes. However, episodes are often similar within a given patient for at least some portion of the lifetime course of illness. As an example, a patient prone to euphoric mania is likely to experience repeated episodes of euphoric mania unless substance abuse, head injury, or duration of illness leads to a change in presentation, such as mania with mixed features (ie, mania with co-occurring depressive symptoms).

Abnormally elevated, expansive, or irritable mood is a core symptom required to diagnose mania [1]. Classic mania is marked by an unusually good, euphoric, or high mood, which may be accompanied by disinhibition (eg, wearing garish clothes or disrobing in public), disregard for social boundaries, expansiveness, and a relentless pursuit of stimulation and social activities (eg, sexual behavior, spending more money than usual, renewing old friendships, or lengthy telephone calls with strangers) [19]. The elevated mood may have an infectious quality that initially engages others; however, patients may appear to be insensitive to the needs of others. As manic episodes worsen, more driven and extreme behavior can emerge.

Another core symptom required to diagnose mania is persistently increased energy and activity [1]. During mania, increased planning and activity is typically marked by impulsivity, poor judgement, and disregard for risks [1,20]. Examples include taking on new and foolish business ventures, unaffordable spending sprees, sexual infidelity or sexual encounters with strangers, and driving recklessly. In addition, patients are often unable to complete the many tasks or projects that are started. Two independent nationally representative surveys in the United States and a third survey in Australia, which identified individuals with mania in the general population, all found that increased activity and energy was the most commonly endorsed symptom [21,22].

Manic patients generally have an exaggerated sense of wellbeing and self-confidence, which may extend to grandiosity of psychotic proportions (see 'Psychosis' below) [1]. As an example, some patients believe they have a special relationship with God or celebrities, or possess talents that surpass the abilities of others. Among individuals with mania in the general population, increased self-esteem and grandiosity are the least commonly endorsed symptom [21,22], consistent with the lack of insight accompanying manic episodes.

In addition, mania is almost universally marked by a decreased need for sleep; this is distinguished from insomnia, which involves the inability to sleep despite feeling tired [1]. Manic patients may feel well-rested, or energetic and "wired," despite sleeping for only a few (eg, three) hours or not all, and patients may not sleep for days without feeling tired [19]. The intensity of this symptom is such that in the premedication era, some patients died from exhaustion.

Common cognitive symptoms of mania include increased mental activity, racing thoughts, distractibility, and difficulty distinguishing between relevant and irrelevant thoughts [1]. These symptoms result in flight of ideas, which are abrupt changes from one topic to another that are usually based upon understandable associations, but may become severe and cause disorganized thoughts [23]. In addition, some patients do not recall events that occur during manic episodes [24]. Other aspects of cognitive impairment are discussed elsewhere in this topic. (See 'Cognition' below.)

Manic speech is generally loud, pressured or accelerated, difficult to interrupt, and may be accompanied by jokes, singing, clanging (choosing words based upon sounds rather than meaning), and dramatic gesticulations. Irritable patients often make hostile comments, swear more than usual, or launch into angry tirades [19].

Psychosocial functioning is markedly impaired, and hospitalization is often required to protect manic patients and prevent behavior leading to painful consequences (eg, financial ruin, job loss, divorce, and assaulting others) [12,25]. One impediment to treatment is that many patients, particularly those who are psychotic, have little insight into their psychopathology and functional impairment, and are impervious to feedback from others [26-28].

An associated feature is that nonpsychotic perception of senses (olfaction, visual acuity, and hearing) is enhanced [1,29].

The course of illness in mania may be marked by a sudden onset, with rapid progression of episodes over a few days. Alternatively, onset of symptoms and progression from hypomania to mania may be relative slow. The duration of manic episodes ranges from weeks to months; in a prospective observational study of 246 manic episodes, the rate of recovery was such that [30]:

- 25 percent of the episodes resolved within 4 weeks of onset
- 50 percent resolved within 7 weeks
- 75 percent resolved within 15 weeks

Following recovery from mania, patients typically do not experience residual symptoms.

Hypomania — Hypomanic episodes (table 2) are characterized by changes in mood, energy, activity, behavior, sleep, and cognition that are similar to those of mania, but less severe [1,31]. Examples include the following:

- Mood during hypomania can be elevated and euphoric, but patients (especially females) commonly experience irritability, dysphoria, and other co-occurring depressive symptoms. In a prospective cohort of patients with bipolar disorder (n >900), most hypomanic episodes were dysphoric [32].

- Self-esteem may be inflated during hypomania, but never reaches the point of delusional grandiosity that can occur during mania.

- Although mental overactivity and flight of ideas can occur in either hypomania or mania, thought form is more organized in hypomania.

- Thinking in hypomania is often quick and may lead to productive increases in goal-directed activities and enhanced creativity, whereas mania is marked by racing thoughts that are disconnected and lead to aimless, ineffective, or destructive behaviors.

- Hypomanic speech can be loud and rapid, but typically is easier to interrupt than manic speech.

- Psychosocial functioning in hypomania is either improved or mildly impaired, whereas mania markedly impairs functioning.

- Risk-taking behavior in hypomania is mild to moderate, but in mania is more severe.

- By definition, psychotic symptoms do not occur in hypomania, and hypomania does not necessitate hospitalization. Patients with psychotic features and patients who require hospitalization are classified as manic. (See 'Mania' above.)

An associated feature of hypomania is that nonpsychotic perception of senses is enhanced [1].

The course of hypomania is such that it generally begins suddenly and progresses quickly over a few days. Episodes typically resolve within several days to weeks; in a prospective observational study of 126 hypomanic episodes, the rate of recovery was such that [30]:

- 25 percent of the episodes resolved within two weeks of onset
- 50 percent resolved within three weeks
- 75 percent resolved within six weeks

Hypomanic symptoms in some patients may be more fleeting than manic symptoms. Nevertheless, hypomanic symptoms must be taken seriously because they indicate increasing instability and the need for treatment.

Major depression — Episodes of major depression (table 3) involve clinically significant changes in mood, behavior, energy, sleep, and cognition [1,6]. The intensity of episodes varies widely.

Similar to unipolar major depression, bipolar major depression is generally characterized by depressed mood, as well as slowing in the pace of mental and physical activity (eg, speech is slow and soft, and output reduced) [6]. Interest or pleasure in usual activities (eg, hobbies) is minimal, energy is low, and memory and concentration are impaired. Appetite is typically diminished and accompanied by weight loss; however, some patients may manifest increased appetite and weight gain. Although behavior is generally slow, some patients are agitated (eg, unable to sit still, wringing their hands, or pacing) [33]. Sleep disturbances (insomnia or hypersomnia) often occur in bipolar depression [34], as do feelings of worthlessness and excessive guilt [6]. Suicidal thoughts and behavior are observed more frequently during major depression than hypomania/mania [35]. (See 'Suicide' below.)

Other clinical features of major depression include poor eye contact, poor hygiene, unkempt appearance, feelings of hopelessness and helplessness, rumination and indecisiveness, negative and nihilistic thoughts, somatic symptoms (eg, pain), and impaired psychosocial functioning [6]. An associated feature is that nonpsychotic perception of senses (eg, olfaction, visual acuity, and hearing) is diminished [29]. Additional information about the clinical manifestation of major depression is discussed elsewhere. (See "Unipolar depression in adults: Clinical features".)

Among patients with bipolar disorder, depressive symptoms occur more often than manic/hypomanic symptoms, especially in bipolar II patients [36,37]. As an example, prospective observational studies examined the mean percent of time that patients had any symptoms of depression or mania/hypomania, including symptoms that met criteria for a mood episode, as well as subthreshold symptoms that did not meet criteria for a full-blown episode. The results included the following:

- Bipolar I disorder (n = 146 and 405) [8,38]

- Depression was present for 32 and 36 percent of follow-up
- Mania/hypomania was present for 9 and 12 percent of follow-up

- Bipolar II disorder (n = 86 and 102) [9,38]

  - Depression was present for 50 and 36 percent of follow-up
  - Hypomania was present for 1 and 10 percent of follow-up

For any given patient, the symptom profile of bipolar major depression is often inconsistent across different episodes. A study of 583 patients with at least two prospectively observed depressive episodes found that within an individual patient, there was little consistency in the specific symptoms or sets of symptoms from one episode to the next [39].

The course of illness in bipolar major depression varies, and onset may be sudden or develop slowly over weeks to months. Episodes typically last several months. A prospective observational study of 373 bipolar major depressive episodes found that the median time to recovery was 15 weeks [30]. In addition, residual symptoms are common among patients who otherwise recover [8,40].

Mixed features — Bipolar episodes of mania, hypomania, and major depression that are accompanied by symptoms of the opposite polarity are referred to as mood episodes with mixed features (eg, hypomania with mixed features or major depression with mixed features) [1]. Other terms used in the literature include mixed episodes, mixed states, mixed mania/hypomania, mixity, and dysphoric mania/hypomania [6,41,42].

- **Mania/hypomania with mixed features** – Manic or hypomanic episodes with mixed features are characterized by episodes that meet full criteria for mania (table 1) or hypomania (table 2), and at least three of the following depressive symptoms during most days of the episode [1]:

  - Depressed mood
  - Diminished interest or pleasure in most activities
  - Psychomotor retardation
  - Low energy
  - Excessive guilt or thoughts of worthlessness
  - Recurrent thoughts about death or suicide, or suicide attempt

  In addition, mania with mixed features is more likely to include clinically significant anxiety or irritability, compared to mania without mixed features [43].

Mania/hypomania with mixed features is common. Multiple studies suggest that among patients with mania/hypomania, mixed features are present in approximately 25 to 30 percent [43,44].

- **Major depression with mixed features** – Bipolar major depressive episodes with mixed features are characterized by episodes that meet full criteria for major depression (table 3), and at least three of the following manic/hypomanic symptoms during most days of the episode [1]:
  - Elevated or expansive mood
  - Inflated self-esteem or grandiosity
  - More talkative than usual or pressured speech
  - Flight of ideas (abrupt changes from one topic to another that are based upon understandable associations) or racing thoughts
  - Increased energy or goal-directed activity
  - Excessive involvement in activities that have a high potential for painful consequences (eg, buying sprees or sexual indiscretions)
  - Decreased need for sleep

  Mixed features appear to be common in patients with bipolar major depression. In a prospective study of more than 900 patients with bipolar disorder who were followed for a median of 15 months across more than 14,000 outpatient visits, depression with mixed features was present in 15 percent of the visits [45].

Compared to bipolar patients without mixed features, patients with mixed features may be at greater risk for comorbid anxiety disorders and substance use disorders [42]. In addition, response to treatment is often poorer in bipolar mood episodes with mixed features than in pure major depression or pure mania [30,42,46].

Mood episodes with mixed features may present de novo or develop during episodes of pure mania, pure hypomania, or pure major depression. Following onset of an episode with mixed features, the mixed feature symptoms may be time limited on a given day, and the three symptoms that constitute the mixed features may vary over the illness episode. Bipolar depressive episodes with mixed features can remit entirely or evolve into pure major depression. Mania with mixed features typically does not transition to pure euphoric mania.

Among patients with bipolar disorder, experiencing mixed features of one polarity appears to increase the risk of mixed features of the opposite polarity. As an example, hypomania with mixed features is more likely to occur in patients who previously had depression with mixed features, compared with patients who have never had depression with mixed features [45].

Psychosis — Manic, major depressive, and mixed episodes may include psychotic features such as [1,6,47,48]:

- Delusions – False, fixed beliefs that can involve grandiose or persecutory convictions, self-referential themes (events, objects, or people have a special significance for the patient), and less commonly, sexual, religious, or political themes.
- Hallucinations – False sensory perceptions that are typically auditory in nature.
- Disorganized thinking and behavior.

It appears that psychosis occurs more often during mania than bipolar major depression [6,48,49], and delusions are observed more often than hallucinations [6,48,50]. By definition, hypomania never includes psychotic features [1].

Psychotic features are common during bipolar mood episodes, such that the lifetime prevalence of psychosis is approximately 60 to 75 percent. A pooled analysis of 33 studies (n >5900 bipolar patients) found a lifetime history of at least one psychotic symptom in 61 percent of patients [6]. Subsequently, a study of bipolar I patients (n >1300) found that the lifetime prevalence of psychotic symptoms was 74 percent [50].

Within a given patient, psychosis often recurs across different mood episodes [48]. However, it is not clear if psychotic features are associated with a more severe long-term course of illness [47,48,51].

Additional information about psychosis is discussed separately. (See "Psychosis in adults: Epidemiology, clinical manifestations, and diagnostic evaluation", section on 'Clinical manifestations'.)

COMORBIDITY

Most adults with bipolar disorder have at least one comorbid psychiatric or general medical illness, and many patients have multiple co-occurring illnesses [52].

Comorbidity in pediatric, geriatric, and rapid cycling bipolar disorder is discussed separately. (See "Pediatric bipolar disorder: Clinical manifestations and course of illness", section on 'Comorbidity' and "Geriatric bipolar disorder: Epidemiology, clinical features, assessment, and diagnosis", section on 'Comorbidity' and "Rapid cycling bipolar disorder: Epidemiology, pathogenesis, clinical features, and diagnosis", section on 'Comorbidity'.)

Psychiatric disorders — Patients with bipolar disorder commonly manifest comorbid psychiatric disorders, including:

- Anxiety disorders
- Attention deficit hyperactivity disorder (ADHD)
- Eating disorders
- Intermittent explosive disorder
- Obsessive-compulsive disorder
- Personality disorders
- Posttraumatic stress disorder (PTSD)
- Substance use disorders

The large majority of bipolar patients have at least one other psychiatric disorder. A large, nationally representative survey found that among individuals with bipolar disorder, the lifetime prevalence of at least one co-occurring disorder was 92 percent [53]. By contrast, the lifetime prevalence of at least one psychiatric disorder in the general population was 46 percent [54].

In addition, many bipolar patients suffer multiple comorbid psychiatric disorders:

- A large, cross-national, epidemiologic survey in 11 countries found that among individuals with bipolar disorder, the lifetime prevalence of three or more comorbid disorders was 44 percent [55].

- An epidemiologic study in the United States found that among individuals with bipolar disorder, the lifetime prevalence of three or more comorbid disorders was 70 percent [53]. By contrast, the lifetime prevalence of three or more psychiatric disorders in the general population was 17 percent [54].

Comorbidity is often associated with a worse course of illness in bipolar disorder, including earlier age of onset, more recurrent mood episodes, and more suicide attempts.

Anxiety disorders — Patients with bipolar disorder frequently suffer comorbid anxiety disorders. As an example, a meta-analysis of 10 community and clinical studies examined the

point prevalence of anxiety disorders among individuals with bipolar disorder (n >2100) who were euthymic at the time of assessment [56]. The primary findings included the following:

- At least one anxiety disorder was present in 35 percent of individuals with bipolar disorder.
- Anxiety disorders occurred five times more often in those with bipolar disorder than population controls (relative risk 5, 95% CI 2-9).
- Bipolar patients manifested the following anxiety disorders, from most to least common:
  - Generalized anxiety disorder
  - Social anxiety disorder (social phobia)
  - Specific phobia
  - Agoraphobia
  - Panic disorder

Compared to bipolar patients without a history of comorbid anxiety disorders, patients with comorbid anxiety have a worse course of illness [57], including:

- Earlier age of onset of bipolar disorder [58,59]
- Decreased likelihood of recovery from mood episodes [57,60]
- More recurrent mood episodes [57,59-62]
- Increased prevalence of substance use disorders [57,58,61]
- Poorer psychosocial functioning [60,61] and quality of life [60,62]
- Poorer insight [57]
- Greater impulsivity [63,64]
- More suicide attempts [58,59,61,62,65-67]

The assessment and diagnosis of anxiety disorders are discussed separately.

- (See "Generalized anxiety disorder in adults: Epidemiology, pathogenesis, clinical manifestations, course, assessment, and diagnosis".)
- (See "Panic disorder in adults: Epidemiology, clinical manifestations, and diagnosis".)
- (See "Social anxiety disorder in adults: Epidemiology, clinical features, assessment, and diagnosis".)
- (See "Specific phobia in adults: Epidemiology, clinical manifestations, course, and diagnosis".)

Attention deficit hyperactivity disorder — Epidemiologic studies show that patients with bipolar disorder often have a history of ADHD:

- A survey in 11 countries found that the lifetime prevalence of ADHD among individuals with bipolar disorder was 20 percent [55].

- A study from the United States found that among individuals with bipolar disorder, the lifetime prevalence of ADHD was 31 percent [53]. By contrast, the lifetime prevalence of ADHD in the general population was 8 percent [54].

Compared with bipolar patients without a history of comorbid ADHD, patients with comorbid ADHD have a worse course of illness, including:

- Earlier age at onset of bipolar disorder [68-71]
- Decreased likelihood of recovery from mood episodes [68]
- More recurrent mood episodes [68,69,71]
- Increased prevalence of anxiety and substance use disorders [68,70]
- Poorer psychosocial functioning [69,70]
- History of legal problems and violence [68,71]
- More suicide attempts [68]

Adult ADHD is discussed separately. (See "Attention deficit hyperactivity disorder in adults: Epidemiology, clinical features, assessment, and diagnosis".)

Eating disorders — Among patients with bipolar disorders, comorbid eating disorders are common and associated with a worse course of illness.

In a meta-analysis of 36 studies that included more than 15,000 patients with bipolar disorder, the lifetime prevalence of co-occurring eating disorders was as follows: [72]:

- Binge-eating disorder – 13 percent
- Bulimia – 7 percent
- Anorexia nervosa – 4 percent

However, heterogeneity across studies was large and nearly all the studies were cross-sectional.

It appears that comorbid eating disorders are observed more often in bipolar patients who are treated in clinical settings, compared with bipolar patients identified in the general population. As an example, a large, nationally representative epidemiologic study of the general population in the United States found that among individuals with bipolar disorder, the estimated lifetime prevalence of binge eating disorder was 3 percent [73].

Compared with bipolar patients without a history of comorbid eating disorders, patients with comorbid eating disorders have a worse course of illness, including:

- Earlier age of onset of bipolar disorder [74,75]
- More recurrent mood episodes [74,75]
- Lifetime history of psychosis [76]
- Increased prevalence of anxiety and substance use disorders [74-77]
- More suicide attempts [74-76]

Eating disorders are discussed separately. (See "Eating disorders: Overview of epidemiology, clinical features, and diagnosis" and "Eating disorders: Overview of prevention and treatment".)

Intermittent explosive disorder — Epidemiologic studies show that in patients with bipolar disorder, approximately 25 to 30 percent suffer comorbid intermittent explosive disorder:

- A survey in 11 countries found that the lifetime prevalence of intermittent explosive disorder among individuals with bipolar disorder was 24 percent [55].

- One study from the United States found that among individuals with bipolar disorder, the lifetime prevalence of intermittent explosive disorder was 29 percent [53]. By contrast, the lifetime prevalence of intermittent explosive disorder in the general population was 5 percent [54].

Intermittent explosive disorder is discussed separately. (See "Intermittent explosive disorder in adults: Clinical features, assessment, and diagnosis" and "Intermittent explosive disorder in adults: Treatment and prognosis".)

Obsessive-compulsive disorder — Obsessive-compulsive disorder appears to be more common among individuals with bipolar disorder than the general population. A pooled analysis of 22 community and clinical studies (number of subjects not provided) estimated that the lifetime prevalence of obsessive-compulsive disorder in bipolar disorder was 14 percent [78]; this compares with a prevalence of 2 percent in the United States population. (See "Obsessive-compulsive disorder in adults: Epidemiology, clinical features, and diagnosis", section on 'Epidemiology'.)

Personality disorders — Personality disorders are more prevalent in bipolar disorder than the general population. A nationally representative survey in the United States found that the one-year prevalence of the following personality disorders was greater among individuals with bipolar disorder than the general population [79]:

- Any personality disorder – 51 percent of bipolar individuals versus 9 percent of the general population

- Paranoid, schizoid, or schizotypal personality disorder (odd or eccentric cluster) – 13 versus 6 percent
- Antisocial, borderline, histrionic, or narcissistic personality disorder (dramatic, emotional, or erratic cluster) – 15 versus 2 percent
- Avoidant, dependent, obsessive compulsive, or passive aggressive personality disorder (anxious or fearful cluster) – 22 versus 6 percent

In addition, personality disorders comorbid with bipolar disorder are common in clinical settings [80]. Multiple studies suggest that among patients with bipolar disorder, the point prevalence of co-occurring personality disorders ranges from approximately 40 to 65 percent:

- A meta-analysis of 13 studies found that in patients with bipolar disorder (n >1100), at least one personality disorder was present in 42 percent [81].
- In a subsequent study of bipolar patients (n >900), the point prevalence of at least one personality disorder was 66 percent [82].

A caveat about diagnosing comorbid personality disorders in a patient with bipolar disorder is that mood symptoms should be fully stabilized before diagnosing a personality disorder. Assessments for personality disorders during a mood episode are associated with substantively greater (inflated) rates of personality disorders [82]. Thus, it is frequently not feasible to diagnose a personality disorder during hospitalization for a bipolar mood episode. The diagnosis of personality disorders is discussed separately. (See "Overview of personality disorders".)

Compared to bipolar patients without a personality disorder, patients with comorbid personality disorders have a worse course of illness, including:

- Earlier age of onset of bipolar disorder [80,82]
- Decreased likelihood of recovery from mood episodes [80,83,84]
- Greater number of manic episodes [82]
- Poorer psychosocial functioning [80]
- More suicide attempts [80]

In addition, personality traits such as novelty seeking and harm avoidance are more common in bipolar patients than healthy controls [85].

Borderline personality disorder — Multiple studies indicate that among individuals with bipolar disorder, borderline personality disorder is comorbid in approximately 20 percent. In a

meta-analysis of 28 hospital-based or population-based studies that included more than 5000 people with bipolar disorder, the prevalence of bipolar disorder was 21.6 percent [86]. However, heterogeneity across studies was large.

Clinicians can screen for comorbid borderline personality disorder by asking about the affective instability criterion [87].

Posttraumatic stress disorder — PTSD commonly co-occurs with bipolar disorder. One literature review noted that the prevalence of comorbid PTSD varies from 4 to 40 percent, and that the prevalence is higher in women than men, and in bipolar I disorder than bipolar II disorder [88]. In addition, the frequency and severity of mood symptoms in patients with bipolar disorder is greater in those with comorbid PTSD than those without PTSD. Comorbid PTSD is also associated with a worse quality of life (subjective satisfaction with one's physical, psychological, and social functioning).

Substance use disorders — Both epidemiologic and clinical studies show that patients with bipolar disorder frequently suffer comorbid substance use disorders, involving drugs such as alcohol, amphetamines, benzodiazepines, cannabis, cocaine, and tobacco [89-91]. Cannabis use may precede or coincide with mania/hypomania, whereas alcohol use may precede or coincide with depression [92,93].

The lifetime prevalence of comorbid substance-related disorders is approximately 50 percent:

- A survey in 11 countries found that the lifetime prevalence of any substance use disorder among individuals with bipolar I disorder was 52 percent, and in bipolar II disorder was 37 percent [55].

- A study from the United States found that among individuals with bipolar I disorder, the lifetime prevalence of substance use disorders was 60 percent, and in bipolar II disorder was 40 percent [53]. By contrast, the lifetime prevalence of substance use disorders in the United States general population was 15 percent [54].

Studies of bipolar patients in clinical settings indicate that comorbid alcohol and drug use disorders are associated with a worse course of illness, including [94-96]:

- More mood symptoms [97-99]
- More hospitalizations [100,101]
- Decreased likelihood of recovery from mood episodes [98,102,103]
- More recurrent mood episodes [90,94,103,104]
- Neurocognitive impairment [105]

- Poorer psychosocial functioning [102,106] and quality of life [107,108]
- Higher levels of aggressiveness [94,109] and more arrests [104,110]
- More suicide attempts [102,111-114]

In addition, comorbid substance use disorders are associated with decreased adherence to treatment for bipolar disorder, which may in part explain the worse course of illness [115,116].

The assessment, diagnosis, and treatment of substance use disorders are discussed separately.

General medical illnesses — Bipolar disorder is associated with an increased risk for comorbid general medical illnesses [117,118], and most patients who present in clinical settings have one or more medical conditions. A study from the Systematic Treatment Enhancement Program for Bipolar Disorder found that among more than 3700 bipolar patients, at least one comorbid medical illness was observed in 59 percent [119]. In other clinical studies of bipolar disorder, the mean number of co-occurring general medical illnesses ranged from 2.4 to 3.4 [107,120-122]. The number and severity of general medical illnesses may increase with age and duration of bipolar disorder [122].

In addition, medical comorbidity is common among the general population of people with bipolar disorder. A nationally representative epidemiologic study found that the prevalence of at least one general medical condition in the past year among individuals with bipolar disorder (n >1500) was 32 percent, and the prevalence of five or more conditions was 10 percent [123].

General medical disorders that appear to be more prevalent among bipolar patients than persons without the disorder include the following [117,118,120,124-131]:

- Relatively common among bipolar patients [117]:
    - Arthritis (eg, rheumatoid arthritis or osteoarthritis)
    - Asthma
    - Cardiovascular disease (angina pectoris, dyslipidemia, hypertension, myocardial infarction, or stroke)
    - Headache (eg, migraine)
    - Thyroid disease (hyperthyroidism or hypothyroidism)
- Less common:
    - Cancer
    - Chronic obstructive pulmonary disease
    - Diabetes
    - Epilepsy

- Gastritis and stomach ulcer
- HIV infection
- Kidney disease
- Liver disease other than cirrhosis (eg, hepatitis C)
- Metabolic syndrome and obesity
- Pain (chronic)
- Parkinson disease
- Vitamin D deficiency

Compared to bipolar patients without a history of comorbid general medical conditions, patients with co-occurring conditions have a worse course of illness, including:

- Decreased probability of recovery from depressive episodes [126]
- More recurrent mood episodes [123,132-134]
- Increased prevalence of anxiety and substance use disorders [123,126,134-137]
- Poorer psychosocial functioning [123,126,136]
- More suicide attempts [137,138]
- Increased all-cause mortality (see 'Mortality' below)

COGNITION

Intelligence quotient (IQ) appears to be largely preserved in bipolar disorder [139-141]. However, many patients manifest deficits in other aspects of cognition, including neurocognitive functioning and social cognition. Cognitive impairments may stem from the primary bipolar disorder or other etiologies such as medications (eg, antipsychotics), comorbidities such as attention deficit hyperactivity disorder or substance use disorders, or physical inactivity [142-144].

Neurocognitive functioning — Multiple studies using standardized tests consistently demonstrate that neuropsychological function in patients with bipolar disorder is often impaired during euthymia as well as mood episodes [139,145-148]. As an example, a meta-analysis of 45 observational studies compared 1423 euthymic bipolar patients with 1524 healthy controls, and found several deficits in patients, including impaired [149]:

- Attention
- Verbal memory
- Executive function (eg, planning, concept or set shifting, and response inhibition)
- Information processing speed

A subsequent meta-analysis of individual patient data (31 studies, 2876 euthymic bipolar patients and healthy controls) that controlled for age, sex, and IQ found that these deficits were clinically small to moderate [150].

However, across different patients with bipolar disorder, neurocognitive function is heterogeneous and ranges from normal to global impairment [143,151]. It is estimated that the type and prevalence of impairment is as follows [142,152]:

- Cognitively intact (little to no impairment) – 30 to 50 percent of patients
- Selective deficits (eg, attention and processing speed) – 30 to 40 percent
- Broad-based deficits (most or all domains) – 10 to 40 percent

Neuropsychological impairment in bipolar disorder is apparent following the first manic episode (but not prior to onset of the disorder) [143,153]. The deficits persist over time and remain stable (rather than progressing) [154-159], are associated with impaired psychosocial functioning and quality of life [142,152,160,161], and overlap with impairments found in schizophrenia and schizoaffective disorder [162-165] as well as unipolar major depression [140,166].

Cognitive impairment in pediatric and geriatric bipolar disorder is discussed separately. (See "Pediatric bipolar disorder: Clinical manifestations and course of illness", section on 'Cognitive impairment' and "Geriatric bipolar disorder: Epidemiology, clinical features, assessment, and diagnosis", section on 'Cognitive impairment'.)

Social cognition — In some patients, bipolar disorder is associated with impaired social cognition or competence [152,167-169]. Social cognition involves the ability to:

- Recognize or infer thoughts, beliefs, and intentions in oneself and others – This knowledge of one's own mind and that of others is often referred to as "theory of mind."
- Identify basic emotions such as happiness, sadness, fear, anger, disgust, and surprise in others (emotion processing or facial expression recognition).
- Make decisions by weighing choices associated with variable rewards and punishments.

A meta-analysis of 20 observational studies (650 euthymic bipolar patients and 607 healthy controls) [167], and a subsequent meta-analysis (18 studies, 1020 patients and controls) [170], found statistically significant, clinically moderate to large deficits in theory of mind, as well as clinically small to moderate impairments in facial emotion recognition [167].

Creativity — The hypothesis that bipolar disorder is associated with creativity is longstanding but not established [6,171,172]. Limited evidence for the association includes studies that found higher scores on creativity measures in bipolar patients than controls, and disproportionately high rates of bipolar disorder in creative individuals or occupations [173-176]. As an example, case control studies based upon national registries identified bipolar patients, healthy siblings of patients, and controls; the results showed that:

- University students who studied artistically creative subjects (eg, visual arts, music, or dance) were more likely to eventually develop bipolar disorder, compared with the healthy siblings (odds ratio 1.3, 95% CI 1.1-1.5) and the general population (odds ratio 1.6, 95% CI 1.5-1.8) [177].

- Bipolar patients were more likely to have worked in creative professions than controls (odds ratio 1.4, 95% CI 1.2-1.5), and siblings were also more likely to have worked in creative professions than controls (odds ratio 1.3, 95% CI 1.2-1.5) [178].

In addition, a population-based study found that the genetic risk for bipolar disorder (based upon multiple genetic markers from genome-wide association data) was greater among creative individuals (eg, actors, dancers, and musicians) than other individuals in the sample, suggesting that the genetic predisposition for bipolar disorder and for creativity may overlap with each other [179,180]. A review hypothesized that one reason the bipolar phenotype persists, despite increased impairment and mortality (see 'Mortality' below), is that bipolar disorder and creativity share genetic factors, which confer an evolutionary advantage to relatives of bipolar patients who are unaffected or do not develop the full illness [181].

LEGAL PROBLEMS

Most patients with bipolar disorder incur criminal justice problems [182]. In a nationally representative survey in the United States [183]:

- The lifetime prevalence of criminal behavior among individuals with bipolar disorder was 69 percent. After adjusting for potential confounding factors (sex, education, and other psychiatric disorders), the analyses found that individuals with bipolar disorder were more than twice as likely to engage in criminal behavior than individuals with no psychiatric disorder (odds ratio 2.2, 95% CI 1.7-2.8).

- The lifetime prevalence of incarceration among individuals with bipolar disorder was 31 percent. After adjusting for potential confounding factors, the analyses found that the risk

of incarceration was one and a half times more likely in those with bipolar disorder than individuals with no psychiatric disorder (odds ratio 1.5, 95% CI 1.1-1.9).

One hypothesis is that incarceration and other legal problems increase as the number of psychiatric hospital beds decreases [184].

VIOLENCE

Patients with bipolar disorder appear to be at an increased risk of being victimized by violence, compared with the general population [185]. However, it is not known if bipolar disorder is associated with an increased risk of perpetrating of violence due to inconsistent results across different studies [186]. Nevertheless, it appears that there is a greater risk that patients will be targets of violence, rather than perpetrators [187,188]. In addition, victimization and perpetration may be related to each other, and patients may exhibit both.

Victimization — A pooled analysis of three observational studies (n = 428 bipolar patients) found that the six-month prevalence of violence victimization was 38 percent [189]. In addition, multiple national registries suggest that after adjusting for potential confounding factors, individuals with bipolar disorder are subjected to violent crime more often than the population without mental disorders [185]. As an example, analyses in one such study found that after controlling for age, sex, and comorbid psychiatric disorders, subjection to violence was three times greater in bipolar patients, compared with their own biologic siblings without psychiatric disorders (hazard ratio 3, 95% CI 2-4) [190].

Patients with bipolar disorder may be the target of violence due to homelessness and comorbid substance use disorders [188]. In addition, untreated symptoms such as psychotic features may provoke violence from others.

Perpetration — Based upon a meta-analysis of 12 studies, it is estimated that the prevalence of violent criminal behavior in patients with bipolar disorder is 7 percent [186]. However, it is not clear whether patients are more likely to perpetrate violence than the general population, due to differences in methods and results across studies:

- Investigators who performed a meta-analysis of 12 studies, which included patients with bipolar disorder (n >58,000) and general population controls (nearly 9 million), concluded that bipolar disorder was not associated with an increased risk of violent criminal behavior [186]. The meta-analysis found that violent criminal behavior was five times more likely in bipolar patients than the general population (odds ratio 5.2, 95% CI 1.3-20.3). However, the comparator group in one of the studies did not have any violent criminal behavior, which

led to a very large odds ratio for that study and likely biased the results of the meta-analysis. When that study was removed in a sensitivity analysis that included the other 11 studies (n >58,000 bipolar patients), the association between bipolar disorder and violent criminal behavior was no longer statistically significant (odds ratio 2.8, 95% CI 0.7-11.3).

- By contrast, other investigators assert that perpetration of violence is greater among bipolar patients than the general population [188,191]. Evidence that supports this hypothesis includes a national registry study of patients with bipolar disorder (n >17,000) and their full biologic siblings without psychiatric disorders; after adjusting for potential confounding factors (eg, age, sex, and comorbid psychiatric disorders), the analyses showed that perpetration of violence was three times greater in patients than the siblings (hazard ratio 3, 95% CI 2-4) [190]. Potential triggers for violent criminality include exposure to violence, substance intoxication, and traumatic brain injury [192].

In a meta-analysis of nine studies that compared bipolar patients and patients with other psychiatric disorders, the risk of violent criminal behavior in the two groups was comparable (odds ratio 0.8, 95% CI 0.4-1.4) [186].

Assessment and management of violent behavior are discussed separately. (See "Assessment and emergency management of the acutely agitated or violent adult".)

MORTALITY

All-cause mortality is increased in bipolar disorder. As an example, national registry studies have found that:

- Life expectancy was approximately nine years shorter in bipolar patients (n >6600) than the general population [193].

- Bipolar disorder was associated with a standardized mortality ratio (number of observed deaths divided by the number of expected deaths) of 3 [194].

Natural causes — In a national registry study, premature mortality in bipolar disorder was related to a two- to three-fold increase in deaths due to coronary heart disease, chronic obstructive pulmonary disease, diabetes mellitus, and influenza or pneumonia [193]. However, mortality from chronic diseases (coronary heart disease, chronic obstructive pulmonary disorder, and diabetes) was lower for bipolar patients who were previously diagnosed with chronic disease than bipolar patients without a prior diagnosis. Thus, identifying and treating chronic diseases in bipolar patients may reduce premature mortality.

Suicide

Attempts — Suicide attempts are common in bipolar disorder. One review that included 26 prospective studies, with follow-up ranging from 1.5 to 44 years, found that suicide attempts occurred in approximately 20 percent of patients [195]. In addition, a study prospectively followed bipolar patients for an average of 16 months, and observed that among 174 patients who attempted suicide, multiple attempts occurred in 32 percent [196].

Literature reviews have found many factors in patients with bipolar disorder that are associated with an increased risk of suicide attempts [197,198]. However, these risk factors are often not consistently associated with attempting suicide across multiple studies, and are likely to have limited predictive power for any specific patient. The following characteristics may have some utility in identifying bipolar patients who are at increased risk of attempting suicide, because the association between the characteristic and attempted suicide is based upon meta-analyses of three or more studies that compared patients who attempted suicide and those who did not:

- Sociodemographic:
  - Female gender [199]
  - Never married (single) [65]
- Clinical:
  - Depressive mood episode [35,199,200]
  - Comorbid psychiatric disorders:
    - Anxiety disorder [65,199]
    - Substance use disorder (eg, alcohol) [65,199]
    - Borderline personality disorder [199]
  - Rapid cycling [65]
  - First degree family history of suicide death [65,199]

The meta-analyses found that the likelihood of suicide attempts was greatest in bipolar patients with a depressive mood episode (odds ratio 6) and comorbid borderline personality disorder (odds ratio 3) [199].

In other studies, increased severity of depressive symptoms was associated with increased intent of suicide or frequency of suicide attempts, regardless of mood episode type such as bipolar depression or bipolar depression with mixed features [35,200].

Other risk factors for suicide attempts in bipolar disorder that have been observed in multiple studies include a history of prior suicide attempt [198], and a history of trauma, such as physical or sexual abuse [65,198,201].

Although younger age of onset of bipolar disorder is repeatedly mentioned as a risk factor for suicide attempts [197,198], its clinical utility is limited because the mean difference between patients who have attempted suicide and those who have not is only three years [65,199].

Additional information about suicidal ideation and behavior is discussed separately. (See "Suicidal ideation and behavior in adults".)

Deaths — Reviews estimate that approximately 10 to 20 percent of bipolar patients die by suicide [197,202]. In addition, multiple studies indicate that the rate of suicide deaths is greater in patients than the general population [195,197,203,204]. As an example, a national registry study examined mortality from suicide in more than six million adults, including patients with bipolar disorder (n >6600) [193]. After adjusting for potential covariates (eg, age, marital status, and substance use disorders), the analyses found that the risk of suicide was approximately five times greater in men with bipolar disorder than other men, and about five times greater in women with bipolar disorder than other women.

The following risk factors may have some utility in identifying bipolar patients who are at increased risk of suicide death, based upon meta-analyses of four or more studies that compared patients who died by suicide and those who did not:

- Male gender (odds ratio 1.5 and 1.8) [65,199]
- History of attempted suicide (odds ratio 2.3) [65]
- First degree family history of suicide death (odds ratio 2.6 and 2.9) [65,199]

Other risk factors for suicide in bipolar disorder that have been observed in multiple studies include hopelessness [65], depressive mood episodes [197,198], and mixed features [197,198].

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: Bipolar disorder (The Basics)")
- Beyond the Basics topics (see "Patient education: Bipolar disorder (Beyond the Basics)")

SUMMARY

- **Diagnosing bipolar disorder** – Diagnosis of bipolar mood episodes and disorders is generally made according to the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR). (See "Bipolar disorder in adults: Assessment and diagnosis".)
- **Clinical presentation of bipolar disorder** – Bipolar disorder can present with mania (table 1), hypomania (table 2), or major depression (table 3). The mood episode at onset of bipolar disorder is usually major depression. (See 'Overview' above and 'Mania' above and 'Hypomania' above and 'Major depression' above.)

  Mania and bipolar major depression are often accompanied by psychotic features, such as delusions (false, fixed beliefs) and hallucinations (false sensory perceptions); by definition, psychosis does not occur in hypomania. (See 'Psychosis' above.)

- **Comorbidity**
  - **Psychiatric** – Most patients with bipolar disorder have at least one comorbid psychiatric illness; common co-occurring disorders include (see 'Psychiatric disorders' above):
    - Anxiety disorders
    - Attention deficit hyperactivity disorder
    - Eating disorders
    - Intermittent explosive disorder
    - Obsessive-compulsive disorder
    - Personality disorders
    - Posttraumatic stress disorder

- Substance use disorders

(See 'Psychiatric disorders' above.)

- **General medical illnesses** – Patients with bipolar disorder are also at increased risk for comorbid general medical illnesses. (See 'General medical illnesses' above.)

- **Neurocognitive function** – Multiple studies using standardized tests in bipolar patients demonstrate that neurocognitive function is generally impaired during asymptomatic phases as well as mood episodes; deficits include impaired attention, verbal memory, executive function, and information processing speed. (See 'Cognition' above.)

- **Violence**

  - **Victimization** – Patients with bipolar disorder appear to be at an increased risk of being victimized by violence, compared with the general population. Also, patients may be victims of violence at rates that are greater than the rate at which they perpetrate violence. (See 'Victimization' above.)

  - **Perpetration** – It is not known if the risk of perpetrating violence is greater in bipolar disorder than the general population, due to inconsistent results across different studies. Aggressive behavior in bipolar disorder and in other psychiatric disorders appears to be comparable. (See 'Perpetration' above.)

- **Suicide**

  - **Attempts** – Suicide attempts are common in bipolar disorder and associated with marital status of never married (single), history of physical or sexual abuse, depressive symptoms, mixed states, progressive severity of depressive episodes, comorbid psychiatric disorders, and family history of suicide death. (See 'Attempts' above.)

  - **Deaths** – Approximately 10 to 20 percent of bipolar patients die by suicide, which is greater than the rate of suicide in the general population. Risk factors for completed suicide include hopelessness and a history of attempted suicide. (See 'Deaths' above.)

ACKNOWLEDGMENT

The UpToDate editorial staff acknowledges Victoria Cosgrove, PhD, who contributed to an earlier version of this topic review.

Topic 14642 Version 29.0