Bipolar disorder in adults: Assessment and diagnosis

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INTRODUCTION

Making the diagnosis of bipolar disorder is often difficult, and following onset of symptoms, many years may elapse until the diagnosis is established [1,2]. As an example, a self-administered survey in 441 bipolar patients found that 35 percent waited at least 10 years between first seeking treatment and receiving the correct diagnosis [3].

This topic reviews the assessment and diagnosis of bipolar disorder in adults. The clinical features 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: Clinical features".)
- (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".)

ASSESSMENT

When to suspect bipolar disorder — Bipolar disorder should be considered in patients who present with symptoms of major depression (table 1), mania (table 2), or hypomania (table 3), including mixed features (ie, symptoms of mood episodes of opposite polarity). (See "Bipolar disorder in adults: Clinical features".)

Initial evaluation — The initial clinical evaluation of patients with a possible diagnosis of bipolar disorder includes a psychiatric and general medical history, mental status and physical examination, and a basic set of laboratory tests (eg, thyroid stimulating hormone, complete blood count, chemistries, and urine toxicology to screen for substances of abuse) [4-6].

The psychiatric history and mental status examination should assess patients for [7]:

- Major depression (table 1)
- Mania (table 2)
- Hypomania (table 3)
- Impulsive or risk-taking behaviors
- Suicidal thoughts and behavior
- Risk factors for suicide attempts and deaths (see "Bipolar disorder in adults: Clinical features", section on 'Suicide')
- Psychotic features (eg, delusions or hallucinations) (see "Bipolar disorder in adults: Clinical features", section on 'Psychosis')
- Comorbid psychiatric and general medical disorders (see "Bipolar disorder in adults: Clinical features", section on 'Comorbidity')

In addition to current symptoms, it is important to ascertain the number, frequency, intensity, and duration of past mood episodes.

Interviewing family members or significant others of patients with a possible diagnosis of bipolar disorder is often helpful [8,9]. Patients may not be forthcoming about suicidal ideation, plans, and attempts; in addition, patients may present with major depression and not recall prior episodes of mania or hypomania, especially if these last occurred several years in the past or with peripartum onset, or were marked by irritability rather than euphoria. Patients who present with mania, hypomania, or psychosis often have poor insight and difficulty providing a history.

Several types of general medical disorders (eg, endocrine or neurologic) can cause bipolar disorder. Findings from the general medical history or physical examination that suggest a general medical condition in patients with bipolar disorder are the same findings that occur in patients without bipolar disorder. Additional laboratory testing, such as brain imaging or electroencephalography (EEG), is guided by abnormal findings in the history and examination

[10-12]. Although neuroimaging studies show abnormalities in different areas of the brain, the only indication for imaging is to rule out disorders that may present with mood symptoms (eg, central nervous system mass, epilepsy, stroke, or trauma) [13,14].

Screening instruments — Although screening for bipolar disorder is often recommended and there are many available instruments [15-18], we suggest not screening because it is not known whether screening improves patient outcomes. In addition, studies in unipolar major depression indicate that screening is beneficial only in settings that can provide follow-up to ensure accurate diagnosis and effective treatment. (See "Screening for depression in adults", section on 'Improved depression outcomes'.)

Nevertheless, the screening tools described in the two subsections immediately below may help educate patients about bipolar disorder.

Mania and hypomania — Bipolar screening instruments do not appear to perform well enough to warrant routine use, particularly in psychiatric outpatients [19]. The most widely used and translated measure that screens for a lifetime history of manic or hypomanic episodes is the 15-item, self-report Mood Disorder Questionnaire (table 4) [15,20-22]. Across multiple studies, the sensitivity of the instrument is such that it fails to identify approximately 33 percent of bipolar patients, and the false positive rate is about 20 percent:

- A pooled analysis of 19 studies (n >3200 patients) conducted in mental health settings found that the sensitivity was 66 percent and specificity was 79 percent [23].
- Another pooled analysis of the questionnaire's operating characteristics in mood disorder specialty clinics found that across 11 studies (n >2000 patients with mood disorders), sensitivity was 65 percent, specificity 81 percent, and positive predictive value 69 percent [24].
- In three studies of unselected, heterogeneous psychiatric outpatients (n >900), sensitivity was 65 percent, specificity was 82 percent, and positive predictive value was 39 percent [24].

The positive predictive values indicate that among psychiatric patients who screen positive for bipolar disorder, many do not have the disorder. Thus, the questionnaire should not be used as a diagnostic proxy for case finding; patients who screen positive require a diagnostic interview to make the diagnosis [25].

Clinicians typically have more difficulty recognizing bipolar II disorder than bipolar I disorder; consistent with this, the Mood Disorder Questionnaire is less effective in screening for bipolar II

disorder than bipolar I disorder [15]. A pooled analysis of 12 studies (n >600 patients) found that the sensitivity for bipolar I disorder was 66 percent, but for bipolar II disorder was only 39 percent [24]. Detecting bipolar II disorder is better accomplished with the 32-item Hypomanic Checklist, which was developed specifically to assess hypomania [23,26], than the Mood Disorder Questionnaire.

In a primary care setting, the sensitivity of the Mood Disorder Questionnaire was fair (58 percent) and specificity excellent (93 percent) [27]. In addition, a pooled analysis of four studies conducted in primary care or general population settings (n >2100 individuals screened) found that the sensitivity and specificity was 43 and 95 percent [23]. Thus, the instrument failed to identify many of the individuals who had bipolar disorder.

Major depression — The Patient Health Questionnaire - 9 Item (PHQ-9) (table 5) is a self-report instrument that can be used to both screen for and diagnose episodes of major depression, and has good psychometric properties [28]. A second option, the Quick Inventory of Depressive Symptomatology – Self-Report 16 Item (QIDS-SR_{16}) (table 6), also has good psychometric properties and is a reasonable alternative [29,30]. The PHQ-9 and QIDS-SR_{16} are discussed separately. (See "Using scales to monitor symptoms and treat depression (measurement based care)", section on 'Patient Health Questionnaire - Nine Item'.)

Diagnostic instruments — Structured and semi-structured, interviewer-administered, diagnostic instruments are available for diagnosing bipolar disorder but are rarely used in routine clinical practice. A structured instrument enables the interviewer to clarify ambiguous or contradictory responses, and may help differentiate the diagnosis of unipolar major depression (major depressive disorder) from bipolar disorder. However, structured instruments are labor intensive and generally reserved for specialized evaluation, treatment, or research settings.

DIAGNOSIS

Diagnosis of bipolar disorder and its subtypes begins by diagnosing the mood episodes that comprise bipolar disorders, and also requires that the clinician exclude other relevant disorders. (See 'Mood episodes' below and 'Bipolar disorders' below and 'Differential diagnosis' below.)

We suggest diagnosing bipolar mood episodes and disorders according to the criteria in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR) [7]. However, a reasonable alternative is the World Health Organization's International Classification of Diseases-10th Revision (ICD-10) [31]. The two sets of criteria are largely the same.

Based upon a meta-analysis of 33 studies (number of patients not provided), the test-retest reliability for diagnosing bipolar disorder is substantial [32]. However, the heterogeneity across studies is very large.

Mood episodes — Bipolar mood episodes include mania, hypomania, and major depression [7].

Mania — The diagnostic criteria for manic episodes are described in the table (table 2). The core symptoms of mania are abnormally and persistently [7]:

- Elevated, expansive, or irritable mood
- Increased energy or goal directed activity

These symptoms occur for at least one week (or any duration if hospitalization is necessary), nearly every day, for most of the day. During this period of mood disturbance and increased energy or activity, at least three (if elated mood predominates) or four (if irritable mood predominates) of the following symptoms must also be present [7]:

- Inflated self-esteem or grandiosity
- Decreased need for sleep (eg, feels rested after three or four hours of sleep)
- More talkative than usual or pressured speech
- Racing thoughts or flight of ideas (abrupt changes from one topic to another that are based upon understandable associations)
- Distractibility
- Increase in goal-directed activity or psychomotor agitation
- Excessive involvement in activities that have a high potential for painful consequences (eg, buying sprees or sexual indiscretions)

Another criterion is that the manic symptoms impair psychosocial functioning, necessitate hospitalization, or are accompanied by psychotic features (eg, delusions or hallucinations); in addition, the symptoms are not the direct result of a substance or general medical condition [7]. (See 'Substance/medication induced bipolar disorder' below and 'Bipolar disorder due to another medical condition' below.)

However, a syndrome of manic symptoms, which emerges during antidepressant treatment (eg, pharmacotherapy or electroconvulsive therapy) and persists beyond the physiologic effect of that treatment, is diagnosed as a manic episode if the minimum criteria for symptoms and duration are met. Manic episodes occur with bipolar I disorder. (See 'Bipolar I disorder' below.)

Additional information about the clinical features of mania is presented separately. (See "Bipolar disorder in adults: Clinical features", section on 'Mania'.)

Hypomania — The diagnostic criteria for hypomanic episodes are described in the table (table 3). Hypomania is characterized by an abnormally and persistently elevated or irritable mood, as well as increased energy or activity, lasting at least four consecutive days, for most of the day, nearly every day [7]. During this period, at least three (if elated mood predominates) or four (if irritable mood predominates) of the additional symptoms that characterize mania must be present. (See 'Mania' above.)

The distinction between hypomanic and manic episodes is based upon the intensity and duration of symptoms. Hypomanic symptoms are less severe than manic symptoms, and the diagnosis of hypomania requires at least four days of symptoms, whereas mania requires at least seven days [7]. In addition, psychosocial functioning in hypomania is either mildly impaired or improved, whereas functioning in mania is markedly impaired. Mania frequently includes psychotic features and leads to hospitalization; by definition, hypomania does not.

Another criterion for hypomania is that the symptoms are not the direct result of a substance [7]. However, a syndrome of hypomanic symptoms, which emerges during antidepressant treatment (eg, pharmacotherapy or electroconvulsive therapy) and persists beyond the physiologic effect of that treatment, is diagnosed as a hypomanic episode if the full criteria for symptoms and duration are met. Hypomanic episodes may occur with bipolar I disorder, bipolar II disorder, or other specified bipolar and related disorder. (See 'Bipolar disorders' below.)

Additional information about the clinical features of hypomania is presented separately. (See "Bipolar disorder in adults: Clinical features", section on 'Hypomania'.)

Major depression — The diagnostic criteria for major depressive episodes are described in the table (table 1). Major depression is characterized by at least five of the following symptoms for at least two weeks; at least one of the symptoms is either dysphoria or anhedonia [7]:

- Depressed mood most of the day, nearly every day (dysphoria)
- Diminished interest or pleasure in nearly all daily activities, most of the day, nearly every day (anhedonia)
- Significant weight loss or weight gain (eg, 5 percent within a month), or decrease or increase in appetite nearly every day
- Insomnia or hypersomnia nearly every day
- Psychomotor agitation or retardation nearly every day
- Fatigue or loss of energy nearly every day

- Thoughts of worthlessness or inappropriate guilt nearly every day
- Diminished ability to think or concentrate nearly every day
- Recurrent thoughts of death or suicidal ideation, or a suicide attempt

In addition, the symptoms cause significant distress or psychosocial impairment, and are not the direct result of a substance or general medical condition. Bereavement does not exclude the diagnosis of a major depressive episode. Major depressive episodes may occur with bipolar I disorder, bipolar II disorder, other specified bipolar disorder, or unspecified bipolar disorder. (See 'Bipolar disorders' below.)

Additional information about the clinical features of bipolar major depression is presented separately. (See "Bipolar disorder in adults: Clinical features", section on 'Major depression'.)

Mood episode specifiers — DSM-5-TR utilizes several terms to specify subtypes of bipolar mood episodes; these terms include [7]:

- **Psychotic features** – Psychotic features include delusions (false, fixed beliefs) and hallucinations (false sensory perceptions), which can occur at any time during a mood episode (see "Psychosis in adults: Epidemiology, clinical manifestations, and diagnostic evaluation", section on 'Clinical manifestations')
- **Catatonia** – Catatonic features are characterized by prominent psychomotor disturbances that occur during most of the episode (see "Catatonia in adults: Epidemiology, clinical features, assessment, and diagnosis")
- **Anxious distress** – Anxious distress is characterized by the presence of two or more of the following symptoms during most days of the mood episode:
  - Tension
  - Restlessness
  - Impaired concentration due to worry
  - Fear that something awful may happen
  - Fear of losing self-control
- **Mixed features** – Episodes of mania, hypomania, and major depression can be accompanied by symptoms of the opposite polarity, and are referred to as mood episodes with mixed features (eg, major depression with mixed features). The optimal definition of

mixed features is not settled. The DSM-5-TR definition is relatively narrow, such that no symptoms that can occur concurrently at both poles can count towards this specifier.

- Manic or hypomanic episodes with mixed features are characterized by episodes that meet full criteria for mania (table 2) or hypomania (table 3), and at least three of the following symptoms during most days of the episode: depressed mood, diminished interest or pleasure in most activities, psychomotor retardation, low energy, excessive guilt or thoughts of worthlessness, and recurrent thoughts of death.

- Major depressive episodes with mixed features are characterized by episodes that meet full criteria for major depression (table 1), and at least three of the following symptoms during most days of the episode: 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), and decreased need for sleep

- **Melancholic features** – Melancholic features are characterized by at least four of the following symptoms during an episode of major depression; at least one of the symptoms is either loss of pleasure or lack of reactivity to pleasurable stimuli:

  - Loss of pleasure in most activities

  - Unreactive to usually pleasurable stimuli (ie, does not feel better in response to positive events)

  - Depressed mood marked by despondency, despair, or gloominess

  - Early morning awakening (eg, two hours before usual hour of awakening)

  - Psychomotor retardation or agitation

  - Anorexia or weight loss

  - Excessive guilt

- **Atypical features** – Atypical features are characterized by at least three of the following symptoms during an episode of major depression; at least one of the symptoms is mood reactivity to pleasurable stimuli:

  - Reactive to pleasurable stimuli (ie, feels better in response to positive events)

- Increased appetite or weight gain
- Hypersomnia (eg, sleeping at least 10 hours per day, or at least 2 hours more than usual when not depressed)
- Heavy or leaden feelings in limbs
- Longstanding pattern of interpersonal rejection sensitivity (ie, feeling deep anxiety, humiliation, or anger at the slightest rebuff from others) that is not limited to mood episodes, and which causes social or occupational conflicts

- **Peripartum onset** – Peripartum onset refers to onset of mood episodes during pregnancy or within four weeks of childbirth (see "Bipolar disorder in postpartum women: Epidemiology, clinical features, assessment, and diagnosis")

Bipolar disorders — The types of bipolar disorder that are described in DSM-5-TR include [7]:

- Bipolar I disorder
- Bipolar II disorder
- Cyclothymic disorder
- Substance/medication induced bipolar disorder
- Bipolar disorder due to another medical condition
- Other specified bipolar disorder
- Unspecified bipolar disorder

Difficulties in diagnosing bipolar disorder may lead clinicians to under diagnose [33-35] or over diagnose [36-38] the disorder. Misdiagnosis is due in part to the overlap between the symptoms of bipolar disorder and the symptoms of other psychiatric disorders, especially unipolar major depression [35,39]. Distinguishing bipolar disorder from other illnesses is discussed elsewhere in this topic. (See 'Differential diagnosis' below.)

Although preliminary neuroimaging studies suggest that structural differences may distinguish patients with bipolar disorder from healthy controls [40], the use of biomarkers to diagnose patients is not standard practice.

Bipolar I disorder — Bipolar I disorder is diagnosed in patients with one or more manic (table 2) episodes [7]. Hypomania (table 3) often occurs as well (table 7). DSM-5-TR stipulates that the mood episodes in bipolar I disorder are not better accounted for by schizoaffective disorder, schizophrenia (table 8), schizophreniform disorder, delusional disorder, or other specified or unspecified schizophrenia spectrum and other psychotic disorder.

Although bipolar I patients nearly always experience at least one episode of major depression, this is not always the case [41]. In a prospective study of 163 bipolar I patients who were followed for 15 to 20 years, manic episodes in the absence of major depression (unipolar mania) was observed in 4 percent [42]. In addition, a nationally representative community survey in the United States identified more than 1400 individuals with bipolar I disorder; unipolar mania (defined as a retrospective report of 10 years of illness with at least three manic episodes and no depression) was present in 5 percent [43].

In diagnosing bipolar I disorder, clinicians can specify whether the course of illness is characterized by rapid cycling or a seasonal pattern, and whether the mood episodes are marked by psychotic features, catatonia, anxious distress, mixed features, melancholic features, atypical features, or peripartum onset [7]. (See 'Mood disorder specifiers' below and 'Mood episode specifiers' above.)

Bipolar II disorder — Bipolar II disorder is diagnosed in patients with a history of at least one episode of hypomania (table 3), at least one episode of major depression (table 1), and no history of mania (table 2) [7]. In addition, the mood episodes in bipolar II disorder are not better accounted for by schizoaffective disorder, schizophrenia (table 8), schizophreniform disorder, delusional disorder, or other specified or unspecified schizophrenia spectrum and other psychotic disorder. Patients with bipolar II disorder are more likely to receive an incorrect diagnosis, compared with bipolar I patients, because hypomania may not be identified by the patients as part of an illness. In addition, clinicians have more difficulty recognizing hypomania than mania.

Differences in the DSM-5-TR criteria for bipolar I disorder and bipolar II disorder are presented in the table (table 7). It is estimated that 5 to 15 percent of patients with bipolar II disorder will eventually suffer an episode of mania and thus change diagnosis to bipolar I disorder [7].

In diagnosing bipolar I disorder, clinicians can specify whether the course of illness is characterized by rapid cycling or a seasonal pattern, and whether the mood episodes are marked by psychotic features, catatonia, anxious distress, mixed features, or peripartum onset [7]. (See 'Mood disorder specifiers' below and 'Mood episode specifiers' above.)

Cyclothymic disorder — Cyclothymic disorder is diagnosed in patients with numerous periods of hypomanic symptoms that fall short of meeting criteria for a hypomanic episode and numerous periods of depressive symptoms that fall short of meeting criteria for a major depressive episode [7]. The symptoms recur over a time interval of at least two consecutive years, during which patients are symptomatic at least half the time and are not symptom-free for more than two consecutive months. In addition, the symptoms cause significant distress or

psychosocial impairment at some point, and are not the direct result of a substance (eg, drug of abuse or medication) or another medical condition. By definition, criteria for major depression, mania, or hypomania have never been met. DSM-5-TR also stipulates that the mood symptoms in cyclothymic disorder are not better accounted for by schizoaffective disorder, schizophrenia (table 8), schizophreniform disorder, delusional disorder, or other specified or unspecified schizophrenia spectrum disorder.

In diagnosing cyclothymic disorder, clinicians can specify whether the mood symptoms are marked by anxious distress [7]. (See 'Mood episode specifiers' above.)

Substance/medication induced bipolar disorder — Substance/medication induced bipolar disorder consists of a mood disturbance that is characterized by a persistently elevated or irritable mood that sometimes is accompanied by depressed mood or diminished interest or pleasure in most activities [7]. The mood disturbance develops during or soon after using substances (eg, phencyclidine or cocaine) or medications (eg, stimulants or corticosteroids) that are capable of producing the symptoms. In addition, the disturbance causes significant distress or impairs psychosocial functioning.

Substance/medication induced bipolar disorder is not diagnosed in the following situations:

- Exposure to antidepressant treatments (eg, pharmacotherapy or to electroconvulsive therapy) that results in episodes of mania or hypomania; these episodes are diagnosed as bipolar I or bipolar II disorder (see 'Bipolar I disorder' above and 'Bipolar II disorder' above)
- The mood disturbance precedes onset of substance intoxication or withdrawal, or exposure to medications
- The disturbance persists for a long period of time (eg, one month) after cessation of acute intoxication or withdrawal (see 'Bipolar I disorder' above and 'Bipolar II disorder' above)
- There is a prior history of recurrent mood episodes
- The disturbance occurs solely during an episode of delirium (see "Diagnosis of delirium and confusional states")

Bipolar disorder due to another medical condition — Bipolar disorder due to a general medical condition consists of a mood disturbance that is characterized by a persistently elevated or irritable mood as well as increased energy or activity [7]. Findings from the history, physical examination, or laboratory tests indicate that the disturbance is caused by another medical condition (eg, hypercortisolism, multiple sclerosis, stroke, traumatic brain injury, or

systemic lupus erythematosus). In addition, the disturbance results in significant distress or impairs psychosocial functioning. Onset of the mood disturbance generally occurs during the first month of the onset of the other medical condition.

Bipolar disorder due to another medical condition is not diagnosed if the mood disturbance precedes onset of the medical condition or occurs solely during an episode of delirium.

Other specified bipolar disorder — Other specified bipolar disorder applies to patients with bipolar symptoms that cause significant distress or impair psychosocial functioning but do not meet the full criteria for a specific bipolar disorder [7]. Clinicians record the diagnosis "other specified bipolar disorder," followed by the reason that the presentation does not meet full criteria for a specific bipolar disorder (eg, other specified bipolar disorder, short duration hypomanic syndromes and major depressive episodes). Examples of syndromes that can be specified when using the diagnosis other specified bipolar disorder include:

- **Short duration hypomanic syndromes (two to three days) and major depressive episodes** – This other specified bipolar disorder diagnosis applies to patients with a lifetime history of at least one major depressive episode who have never met full criteria for mania or hypomania, but have experienced two or more periods that lasted for only two or three days and met full criteria for a hypomanic episode, except for the duration criterion of four days. These short duration hypomanic syndromes do not overlap in time with the major depressive episodes, so the disorder is not diagnosed as major depressive episode with mixed features.

- **Hypomanic symptoms and major depressive episodes** – Other specified bipolar disorder applies to patients with a lifetime history of at least one major depressive episode who have never met full criteria for mania or hypomania, but have experienced at least one period that lasted for at least four consecutive days, during which the patient had hypomanic symptoms insufficient in number to meet full criteria for a hypomanic episode. These hypomanic symptoms do not overlap in time with the major depressive episodes, so the disorder is not diagnosed as major depressive episode with mixed features.

- **Hypomanic episodes without prior major depressive episode** – Patients with a lifetime history of one or more hypomanic episodes, who have never met full criteria for mania or major depression, are diagnosed as other specified bipolar disorder, hypomanic episodes without prior major depression.

- **Short duration cyclothymia** – Patients who meet criteria for cyclothymic disorder with the exception that the syndrome has lasted for less than two consecutive years are diagnosed as other specified bipolar disorder, short duration cyclothymia.

Unspecified bipolar disorder — Unspecified bipolar disorder applies to patients with bipolar symptoms that cause significant distress or impair psychosocial functioning but do not meet the full criteria for a specific bipolar disorder [7]. This diagnostic category is used when clinicians decide not to specify the reason that the presenting syndrome does not meet the full criteria for a specific bipolar disorder, and can include situations in which there is insufficient information to make a more specific diagnosis (eg, in the emergency department).

Mood disorder specifiers — DSM-5-TR uses the following terms to specify the course of illness in bipolar I or II disorder [7]:

- **Rapid cycling** – Rapid cycling is defined as four or more mood episodes (mania, hypomania, or major depression) during a 12-month period (see "Rapid cycling bipolar disorder: Epidemiology, pathogenesis, clinical features, and diagnosis")

- **Seasonal pattern** – Seasonal pattern refers to a regular temporal relationship between the onset of at least one type of mood episode (mania, hypomania, or major depression) and a particular time of year, for the past two years. Remission (or change in polarity) also occurs at a specific time of year. The other types of episodes need not follow a seasonal pattern. As an example, episodes of bipolar II major depression may begin each winter and remit in spring, whereas hypomanic episodes do not occur at one specific time of year. In addition, the lifetime number of seasonal manic, hypomanic, or depressive episodes substantially outnumbers the nonseasonal episodes.

  Seasonal pattern is not used as a specifier if a type of mood episode occurs in response to a seasonally related psychosocial stressor (eg, unemployment every winter), or if episodes occur at other times of the year as well as seasonally. A seasonal pattern may be more common in bipolar II disorder than bipolar I disorder.

  In bipolar disorder with seasonal pattern, depressive episodes occur more often in winter than summer [44]. By contrast, hypomanic/manic episodes occur more often in spring and summer, compared with fall and winter.

Diagnostic hierarchy and change — The bipolar disorders form a hierarchy, and the specific disorder that is diagnosed may change over time, depending upon the course of illness [7]:

- Both other specified bipolar disorder and unspecified bipolar disorder can change to cyclothymic disorder if the symptoms persist for two consecutive years and other criteria for cyclothymia are met. Once cyclothymic disorder is diagnosed, the diagnosis never reverts back to other specified bipolar disorder or unspecified bipolar disorder.

- Patients with other specified bipolar disorder or unspecified bipolar disorder who suffer episodes of hypomania and major depression are reclassified as bipolar II disorder. Once bipolar II disorder is diagnosed, the diagnosis never reverts back to other specified bipolar disorder or unspecified bipolar disorder, regardless of future course of illness.

- Patients with other specified bipolar disorder, unspecified bipolar disorder, cyclothymic disorder, or bipolar II disorder who experience manic episodes are reclassified as bipolar I disorder; patients diagnosed with bipolar I disorder retain this diagnosis indefinitely.

- Patients with cyclothymic disorder who develop a major depressive episode are reclassified as unipolar major depression (major depressive disorder) (see "Unipolar depression in adults: Assessment and diagnosis"), and patients with cyclothymic disorder who develop a hypomanic episode are reclassified as other specified bipolar disorder, hypomanic episode without prior major depressive episode. In both situations, the cyclothymic disorder diagnosis is dropped.

There are no established predictors of diagnostic change. As an example, it is not clear which bipolar II patients will incur mania and change diagnosis to bipolar I disorder.

In addition, patients who are initially and correctly diagnosed with bipolar disorder may eventually change diagnosis to a different disorder [45]. In an observational study of 95 bipolar patients with psychotic features who were prospectively followed for up to 10 years, the diagnosis changed in 22 percent (primarily to schizophrenia) [46].

Presenting the diagnosis to patients — When first discussing the diagnosis of bipolar disorder with patients and families, we seek to educate them and bring perspective to some of the media presentations of the illness. One metaphor that we find helpful is to use epilepsy as a model: bipolar disorder is a brain illness that most patients can effectively manage with medications, education about the disorder (psychoeducation), and healthy lifestyles (eg, exercise and diet). Like epilepsy, patients with bipolar disorder may be "well" when stabilized, but if medications are stopped, particularly abruptly, patients are at increased risk of recurrent mood episodes over the next weeks to months [47]. In addition, both epilepsy and bipolar disorder are lifelong brain illnesses that need ongoing care and attention.

Other useful first remarks concern the importance of avoiding use, especially excessive use, of psychoactive substances such as alcohol, cannabis, or psychedelics. The use of substances may lead to a more treatment-resistant form of the illness. We also discuss the importance of maintaining stable circadian rhythms (eg, sleep), and usually encourage patients to participate in patient advocate organizations such as the Depression Bipolar Support Alliance.

DIFFERENTIAL DIAGNOSIS

Symptoms of bipolar disorder in adults can overlap with symptoms of other psychiatric disorders, which need to be considered to prevent inappropriate treatment. Some of these other disorders may be comorbid with bipolar disorder (eg, substance use disorders, attention deficit hyperactivity disorder, and borderline personality disorder) [48,49]. The differential diagnosis of bipolar disorder in children, adolescents, and geriatric patients is discussed separately. (See "Pediatric bipolar disorder: Assessment and diagnosis", section on 'Differential diagnosis' and "Geriatric bipolar disorder: Epidemiology, clinical features, assessment, and diagnosis", section on 'Differential diagnosis'.).

Unipolar major depression — Episodes of major depression occur in both unipolar major depression (major depressive disorder) and bipolar disorder; however, patients with bipolar disorder have a lifetime history of manic/hypomanic episodes (table 2 and table 3), whereas patients with unipolar major depression do not [7]. Nevertheless, bipolar disorder is often misidentified as unipolar major depression [50-55] because the mood episode at onset of bipolar disorder is often a depressive episode [56-58], multiple episodes of major depression may occur prior to the first lifetime episode of mania or hypomania [59], and depressive symptoms occur more frequently than mood elevated symptoms [60,61]. In addition, clinicians and patients may not recognize mania/hypomania due to the presence of comorbid disorders [62,63], and patients often underreport mania/hypomania (eg, episodes that occurred years earlier may be forgotten or not be recognized as part of an illness) [3].

The diagnostic criteria for bipolar major depression and unipolar major depression are similar and there are no pathognomonic signs that distinguish the two [7,64]. However, replicated findings suggest that the following symptoms may be more common in bipolar depression than unipolar depression [64-72]:

- Psychotic features such as delusions and hallucinations; psychotic features that occur as part of bipolar depression are pathognomonic of bipolar I disorder
- Atypical depressive features such as hypersomnia, hyperphagia, and leaden paralysis (limbs feel heavy as though made of lead and are difficult to move)

In addition, a nationally representative survey that compared bipolar disorder (n = 1429 individuals) with unipolar major depression (n = 5695 individuals) found that [67]:

- The first lifetime depressive episode occurred six years earlier in bipolar disorder than in unipolar depression (mean age 24 versus 30 years)

- Prevalence of comorbid anxiety, substance use, and personality disorders was greater in bipolar disorder than in unipolar depression
- Social functioning was poorer in bipolar disorder than in unipolar depression

Multiple studies have found that the following clinical features may be more common in patients with unipolar major depression who eventually experience mania/hypomania and change diagnosis to bipolar disorder, compared with unipolar depressed patients who do not change diagnosis [7,64,71,73-76]:

- Subthreshold manic/hypomanic symptoms, that is, mood elevated symptoms not meeting syndromal criteria for mania or hypomania. (Patients with this presentation may meet criteria for unipolar major depression with mixed features.)
- Younger age of onset of first lifetime episode of major depression (eg, age <25 years)
- Family history of bipolar disorder
- Multiple (eg, at least three to five) recurrences of major depression
- Poor response to antidepressants (eg, failure to respond to at least two treatment trials)

Other clinical features that may be greater in bipolar disorder than unipolar major depression are comorbid mental disorders (eg, anxiety disorders, substance use disorders, and personality disorders), as well as impulsivity, aggression, and hostility [71].

Although preliminary studies suggest that biomarkers may distinguish bipolar depression from unipolar depression, the use of biomarkers to differentiate depressive syndromes is not standard practice. Examples of investigated biomarkers include central nervous system functioning (eg, cerebral blood flow and glucose metabolism), white matter connectivity, and gray and white matter volumes [2,77-80], as well as brain derived neurotrophic factor gene expression and serum concentrations [81].

The diagnosis of unipolar major depression is discussed separately. (See "Unipolar depression in adults: Assessment and diagnosis", section on 'Unipolar major depression'.)

Schizoaffective disorder — Schizoaffective disorder and bipolar I disorder are both characterized by manic and major depressive episodes, as well as psychotic symptoms (eg, delusions and hallucinations), agitation, irritability, and catatonia [7]. However, the two disorders differ in the timing of psychotic symptoms. In bipolar I disorder, psychosis occurs only

in the context of mania or major depression; by contrast, psychosis in schizoaffective disorder can and does occur in the absence of mood episodes.

Schizophrenia — Schizophrenia (table 8) and bipolar disorder may both manifest psychosis as well as episodes of major depression [7]. The primary distinguishing feature is that in schizophrenia, psychotic symptoms occur in the absence of prominent mood symptoms; in bipolar disorder, psychosis occurs only during manic or major depressive episodes. In addition, neurologic soft signs (eg, subtle impairment of motor coordination and sequencing of complex motor tasks) may be more prominent in schizophrenia than bipolar disorder [82].

The diagnosis of schizophrenia is discussed separately. (See "Schizophrenia in adults: Clinical features, assessment, and diagnosis", section on 'Diagnosis'.)

Attention deficit hyperactivity disorder — Symptoms that are common to both attention deficit hyperactivity disorder (ADHD) and mania/hypomania include impaired attention and concentration; distractibility and frequent changes in activity or plans; difficulty with task completion; increased activity, restlessness, and talking; and disinhibited and inappropriate behavior [83-85]. However, mania is accompanied by inflated self-esteem and grandiosity, flight of ideas (abrupt changes from one topic to another that are based upon understandable associations), decreased need for sleep, and excessive involvement in pleasurable activities; these symptoms do not occur in ADHD [7]. In addition, major depression nearly always occurs in bipolar disorder, but is absent in ADHD. The diagnosis of ADHD is discussed separately. (See "Attention deficit hyperactivity disorder in adults: Epidemiology, clinical features, assessment, and diagnosis".)

Borderline personality disorder — The alternating mood syndromes ("mood swings") and irritability of bipolar disorder can resemble the affective instability and uncontrolled anger of borderline personality disorder [86-89]. Recurrent suicidal ideation and behavior, problematic impulsive behaviors (eg, excessive spending sprees, sexual promiscuity, substance abuse, and reckless driving), and poor psychosocial functioning are also common to bipolar disorder and borderline personality disorder [7]. However, several clinical features distinguish the two disorders [7,90]:

- The depressive or mood elevated syndromes in bipolar disorder are longer in duration (eg, lasting days to weeks) compared with the labile affective states of borderline personality disorder (eg, lasting minutes to hours)
- Bipolar mood syndromes are less connected to events in the environment; by contrast, the mood lability of borderline personality disorder is often triggered by stressors such as perceived rejection or failure

- A family history of bipolar disorder in first degree relatives suggests bipolar disorder rather than borderline personality disorder

- Borderline personality disorder is marked by unstable and intense interpersonal relationships, identity disturbance (fluctuating self-image or sense of self), chronic feelings of emptiness, and frantic efforts to avoid abandonment; these features are not characteristic of bipolar disorder

The diagnosis of borderline personality disorder is discussed separately. (See "Borderline personality disorder: Epidemiology, pathogenesis, clinical features, course, assessment, and diagnosis", section on 'Diagnosis'.)

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: Bipolar disorder".)

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

- **Diagnosis is often delayed** – After onset of bipolar disorder, difficulties in making the diagnosis often leave patients waiting for years to receive the correct diagnosis. (See 'Introduction' above.)

- **Initial evaluation** – The initial clinical evaluation of patients with a possible diagnosis of bipolar disorder includes a psychiatric and general medical history, mental status and physical examination, and focused laboratory tests. The psychiatric history and mental status examination should include questions about major depression (table 1), mania (table 2), hypomania (table 3), suicidal ideation and behavior, psychotic features (delusions or hallucinations), and comorbid psychiatric and general medical disorders. (See 'Assessment' above.)

- **Screening** – Although screening for bipolar disorder is often recommended, we suggest not screening because it is not known whether screening improves patient outcomes. It is also not clear that bipolar screening instruments perform well enough to warrant routine use. (See 'Screening instruments' above.)

- **Making the diagnosis**

  - **Bipolar mood episodes** – The American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR) is generally used to diagnose bipolar mood episodes, including mania (table 2), hypomania (table 3), and major depression (table 1). (See 'Mood episodes' above.)

  - **Bipolar I disorder** – Bipolar I disorder is diagnosed in patients with one or more manic episodes. Nearly all patients suffer at least one episode of major depression, and hypomania often occurs as well. (See 'Bipolar I disorder' above.)

  - **Bipolar II disorder** – Bipolar II disorder is diagnosed in patients with a history of at least one hypomanic episode and at least one major depressive episode, and no history of manic episodes. (See 'Bipolar II disorder' above.)

  - **Cyclothymic disorder** – Cyclothymic disorder is diagnosed in patients with periods of hypomanic symptoms that fall short of meeting criteria for a hypomanic episode, and periods of depressive symptoms that fall short of meeting criteria for a major depressive episode. Symptoms recur over a time interval of two or more consecutive years, during which patients are symptomatic at least half the time and are not symptom-free for more than two consecutive months. (See 'Cyclothymic disorder' above.)

- **Other specified/unspecified bipolar disorder** – Patients with bipolar symptoms that cause significant distress or impair psychosocial functioning but do not meet the full criteria for a specific bipolar disorder are diagnosed with either other specified bipolar disorder, or with unspecified bipolar disorder, depending upon whether clinicians choose to specify the reason that the presenting syndrome does not meet criteria for a specific bipolar disorder. (See 'Other specified bipolar disorder' above and 'Unspecified bipolar disorder' above.)

- **Differential diagnosis** – The differential diagnosis of bipolar disorder includes unipolar major depression, schizoaffective disorder, schizophrenia, attention deficit hyperactivity disorder, and borderline personality disorder. (See 'Differential diagnosis' above.)

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