# DIAGNOSING BIPOLAR DISORDER IN PRIMARY CARE*

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## ABSTRACT

Because of the current structure of our healthcare system and the societal stigma regarding some psychiatric illnesses, the diagnosis and management of a patient with a bipolar disorder often rests on the shoulders of the primary care physician. Bipolar depression is under-recognized and underdiagnosed in both primary care and psychiatry. For primary care physicians, there are 2 main challenges in diagnosing bipolar disorder: distinguishing unipolar from bipolar depression and eliciting a past history of manic or hypomanic symptoms. This article will review the presentation of bipolar disorder and the differentiating features from its most common misdiagnoses, unipolar depression and anxiety. Methods for eliciting a history of hypomania or mania are also discussed. Many primary care physicians may never feel comfortable diagnosing or treating bipolar disorder. In these instances, and in complex or refractory cases, or in the setting of significant suicidal ideation or behavior, the patient should be referred to a psychiatrist for a full evaluation and for ongoing care. Detecting bipolar disorder and differentiating bipolar from unipolar depression is essential because of the treatment implications and severe morbidity and mortality associated with bipolar disorder. In any patient with depressive symptoms, the primary care physician should inquire about past and present symptoms of (hypo)mania, inquire about a family history of bipolar disorder, recognize the depressive symptoms that are common in bipolar depression, inquire about suicidal thoughts or plans, and realize that mood disorders impact on physical and cognitive health and overall level of function, as well as mood.

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Bipolar disorder is one of the more severe psychiatric disorders, in part because of the risk of psychosis, association with severe depressions that are often disabling and accompanied by suicidal thoughts or behavior, and explosive quality of a manic episode, during which a patient can, within a brief period of time, engage in behaviors with severe adverse consequences for themselves and their families. Many practitioners also perceive bipolar disorder as being difficult to diagnose. However, bipolar disorder, like other psychiatric disorders, can be diagnosed very reliably by experienced and well-trained clinicians.

In its classic form, bipolar disorder, in general, and mania, in particular (Table 1), has a unique presentation, which is consistent historically and cross-culturally.[1] However, bipolar disorder can also be viewed as a spectrum of disorders, rather than a single illness. Problems with diagnosis occur in regard to those forms of bipolar disorder at the edges of the spectrum, as well as in differentiating unipolar, or major, depression (in which the patient never has hypomanic or manic episodes) from bipolar depression. With regard to the former, the validity of bipolar spectrum disorders is

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debated within the psychiatric community. Although different investigators have used somewhat different criteria for bipolar spectrum disorders, they are usually characterized by episodes that fall just short of satisfying the duration or severity criteria for a hypomanic episode, as defined in *The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (DSM-IV-TR), outlined in Table 2.[1-4]

Unfortunately, psychiatry is often considered a separate discipline from other areas of medicine—a notion further suggested by the frequent physical separation of psychiatric facilities from hospitals, clinics, and physician offices. While many patients with unipolar depression are managed in a primary care setting, many cases of bipolar depression are under-recognized or misdiagnosed, so these patients may be inadvertently treated by primary care physicians for another disorder. Many primary care physicians may never feel comfortable diagnosing bipolar disorder. In those instances, and in the case of any complex or refractory patient, or significant suicidal ideation or behavior, the patient should be referred to a psychiatrist for a full evaluation and for ongoing care. However, not uncommonly, the patient does not follow through with this referral. This may be due to insurance restrictions, stigma associated with psychiatric care, or inconvenience (ie, separation of psychiatry from general medicine/having to go to another facility for treatment). Thus, the diagnosis and management of a patient with a bipolar disorder may come to rest on the shoulders of the primary care physician.

Bipolar depression is under-recognized and underdiagnosed in primary care and psychiatry. For primary care physicians, there are 2 main challenges in diagnosing bipolar disorder: distinguishing unipolar from bipolar depression and eliciting a history of past manic or hypomanic symptoms. It is helpful to remember that mood disorders are not just about mood: there are associated physical, cognitive, and behavioral symptoms that often point to the correct diagnosis.

**Table 1. Summary of DSM-IV-TR Criteria for a Manic Episode**

A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting >1 week (or any duration of hospitalization is necessary)

B. During the period of mood disturbance, at least 3 of the following symptoms have persisted (4 if irritable mood is only irritable) and have been present to a significant degree:
   1. Inflated self-esteem or grandiosity
   2. Decreased need for sleep (eg, feels rested after only 3 hours of sleep)
   3. More talkative than usual or pressure to keep talking
   4. Flight of ideas or subjective experience that thoughts are racing
   5. Distractibility (ie, attention too easily drawn to unimportant or irrelevant external stimuli)
   6. Increase in goal-directed activity (socially, at work or school, or sexually) or psychomotor agitation
   7. Excessive involvement in pleasurable activities that have a high potential for painful consequence (eg, engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)

C. The symptoms do not meet criteria for a mixed episode

D. The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, to necessitate hospitalization to prevent harm to self or others, or there are psychotic features

E. The symptoms are not due to the direct physiological effects of a substance (eg, a drug of abuse, a medication, or other treatment) or a general medical condition (eg, hyperthyroidism)

DSM-IV-TR = *The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision.*

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## Diagnostic Criteria for Bipolar Disorders

Bipolar disorders are depressive disorders defined by at least 1 major depressive episode and at least 1 episode of mania or hypomania. The spectrum of bipolar disorders ranges from the most severe form (bipolar disorder type I [BP-I]) to a milder form (BP-II) to cyclothymic disorder. BP-I is characterized as at least 1 manic episode, usually accompanied by depressive episodes; the latter are more common in most patients.[1] BP-II is defined as at least 1 episode of major depressive disorder (MDD) and at least 1 hypomanic episode.[1]

### *Mania and Hypomania*

Tables 1 and 2 outline the DSM-IV-TR criteria for manic and hypomanic episodes.[1] Regarding the manic episode criteria, there are several features to note. A manic episode refers to a complex of symptoms co-occurring over a distinct period of time. It is distinguished from hypomania by duration of the episode (minimum of 4 vs 7 days) and the degree of impair-

ment (marked, causing hospitalization, or accompanied by psychosis in the case of mania versus noticeable to others in the case of hypomania). Although the precise onset or offset of a hypomanic or manic episode may be difficult to discern, criterion A specifies that the manic or hypomanic symptoms should occur during a "distinct period" (ie, they should be distinguishable from the patient's baseline level of function). One of the most familiar characteristics of a (hypo)manic (in this article, [hypo]manic is used to mean hypomanic or manic) episode is elevated, expansive, or euphoric mood. Although this is a classic presentation, (hypo)mania can also present as irritability and agitation; indeed, even a euphoric manic patient demonstrates prominent irritability when his or her intense desire to pursue an unrealistic goal is thwarted. Because (hypo)mania may be characterized by irritability and agitation, it is often mistaken for anxiety or depression. To make the correct diagnosis, the physician must perform a careful assessment of all associated symptoms of hypomania and mania (Tables 1 and 2), in addition to the symptoms of anxiety, depression, and other major psychiatric illnesses, the patient's personal and family history of psychiatric illness, and the context in which the symptoms occur. Because of the complexity of this differential diagnosis, its treatment implications, and the potential adverse consequences of misdiagnosis, consultation with a psychiatrist is strongly recommended.

In addition to the presence of euphoria, patients with (hypo)mania can present with several other symptoms that are rarely, if ever, seen in other psychiatric illnesses. These include decreased need for sleep, excessive pleasure seeking, and increased goal-oriented activity. Importantly, the insomnia of a (hypo)manic episode is characterized by decreased need for sleep, not by simply being unable to sleep. Patients experiencing (hypo)mania can get by on just a few hours of sleep and not feel tired. In contrast, depressed patients experiencing insomnia would prefer to sleep if they could. (Hypo)mania is also characterized by excessive pleasure seeking and increased goal-directed behavior (these both should be increased relative to a patient's usual baseline behavior). Excessive pleasure seeking often manifests as the pursuit of pleasure without regard to potential adverse consequences (ie, hypersexuality and spending money). Thus, in the course of an acute manic episode, it is not uncommon for patients to bankrupt themselves and their families, or to engage

**Table 2. Summary of DSM-IV-TR Criteria for a Hypomanic Episode**

A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting throughout at least 4 days, that is clearly different from the usual nondepressed mood

B. During the period of mood disturbance, at least 3 of the following symptoms have persisted (4 if irritable mood is only irritable) and have been present to a significant degree:
   1. Inflated self-esteem or grandiosity
   2. Decreased need for sleep (eg, feels rested after only 3 hours of sleep)
   3. More talkative than usual or pressure to keep talking
   4. Flight of ideas or subjective experience that thoughts are racing
   5. Distractibility (ie, attention too easily drawn to unimportant or irrelevant external stimuli)
   6. Increase in goal-directed activity (socially, at work or school, or sexually) or psychomotor agitation
   7. Excessive involvement in pleasurable activities that have a high potential for painful consequence (eg, engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)

C. The episode is associated with an unequivocal change in functioning that is uncharacteristic of the person when not symptomatic

D. The disturbance in mood and the change in functioning are observable by others

E. The episode is not severe enough to cause marked impairment in social or occupational functioning or to necessitate hospitalization, and there are no psychotic features.

F. The symptoms are not due to the direct physiological effects of a substance (eg, a drug of abuse, a medication, or other treatment) or a general medical condition (eg, hyperthyroidism)

Note: Hypomanic-like episodes that are clearly caused by somatic antidepressant treatment (eg, medication, electroconvulsive therapy, and light therapy) should not count toward a diagnosis of bipolar disorder II.
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**Table 3. Mania Versus Hypomania**

| | Episode duration | Impairment |
|---|---|---|
| Mania | ≥7 days | Marked<br>Hospitalization<br>Psychosis |
| Hypomania | ≥4 days | Noticeable to others |

in behavior that is profoundly upsetting to them later.

For a diagnosis of mania, only 1 episode is required and an essential criterion is marked impairment. Mania is sometimes, and hypomania is often, a positive experience, and so it may not be reported to the physician. As will be discussed later in this article, it may be necessary to measure impairment by the impact of the patient's behavior on family and friends. Although, in DSM-IV, hospitalization is viewed as a measure of impairment, this can be misleading because hospitalization can be driven more by insurance coverage than impairment.

Hypomania is distinguished from mania by lesser severity and shorter duration (Table 3). Whereas mania has to cause marked impairment hypomania only has to be noticeable to others. Thus, it can be difficult to obtain a history of hypomania because patients often do not report it because they feel better, and may be more productive, than usual.[5] When patients do present to a physician, it is almost always for a depressive episode, and they are then frequently misdiagnosed as having unipolar depression.

### *Major Depressive Disorder*

The hallmark symptoms of depression, unipolar or bipolar, are anhedonia (the inability to experience pleasure) and dysphoric, sad mood; patients must experience one of these to meet criteria for the illness. In addition, although irritability is a frequent symptom of depression in adults, it is a criterion for MDD only in children (Table 4).[1] This discrepancy in diagnostic criteria may be due to differences in history taking between adult and pediatric patients. In pediatric patients, history of the symptoms and signs of depression is obtained from other sources (usually, parents), but, for adults, information is rarely obtained from sources other than the patient. In other words, irritability is often not reported by patients themselves, but instead by the individuals who live with them. Spouses, friends, and family members often provide important clues to diagnosis because they report behavioral changes which the patient may be embarrassed to admit, or of which the patient may not be cognizant. During the history taking, the physician should ask the patient if others have commented on the patient's behavior (eg, "Have people mentioned that you're not acting like yourself lately?"). Also, as with mania and hypomania, impairment is an important criterion and affects decisions about treatment.

### Bipolar Spectrum Illnesses

Cyclothymic disorder is an even milder form of bipolar disorder than BP-II. As summarized in Table

**Table 4. Summary of DSM-IV-TR Criteria for a Major Depressive Episode**

A. Five or more of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least 1 of the symptoms is depressed mood or loss of interest or pleasure:
   1. Depressed mood most of the day, nearly every day, as indicated by subjective report (eg, feels sad or empty) or observation made by others (eg, appears tearful). Note: In children and adolescents, can be irritable mood.
   2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by subjective account or observation made by others).
   3. Significant weight loss when not dieting or weight gain (eg, a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. Note: In children, consider failure to make expected weight gains.
   4. Insomnia or hypersomnia nearly every day.
   5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
   6. Fatigue or loss of energy nearly every day.
   7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
   8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (by subjective account or as observed by others).
   9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

B. The symptoms do not meet the criteria for a mixed episode

C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning

D. The symptoms are not due to the direct physiological effects of a substance (eg, a drug of abuse or a medication) or a general medical condition (eg, hypothyroidism)

E. The symptoms are not better accounted for by bereavement (ie, after the loss of a loved one, the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation)

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5, it is characterized by numerous periods of hypomanic symptoms and numerous periods of depressive symptoms that do not meet criteria for MDD, for at least 2 years.[1] It is a chronic disorder, with no asymptomatic periods longer than 2 months, and it can cause clinically significant distress or impairment. Of note, cyclothymic disorder develops into BP-I or BP-II in 15% to 50% of patients.[1] Unfortunately, there are very few data regarding treatment for cyclothymic disorder. Often, the treatment of cyclothymic disorder is similar to that of BP-II, but in most instances the PCP will want to obtain a psychiatric consultation to confirm the diagnosis and recommend treatment.

Bipolar disorder, not otherwise specified, refers to mood disorders that appear to be bipolar in nature but do not fulfill the criteria for any of the other bipolar disorders. These can include periods of manic or hypomanic symptoms without any depressive episodes, shorter episodes of elevated mood (ie, fewer than 4 days), or periods of elevated mood that cannot be verified by others or are not noticed by others.[1]

Amongst psychiatric researchers, the concept of temperament and the influence of personality type on affective disorders is currently a matter of some debate. In 1921, Kraepelin first described 4 affective temperaments: hyperthymic, dysthymic, cyclothymic, and irritable.[6] As summarized in Table 6, there is significant overlap among them.[7] Temperaments are affective styles that are lifelong and often do not cause significant impairment.[8] The hyperthymic temperament, which may be viewed as a chronic, mild hypomania, might characterize many politicians, entrepreneurs, or other highly motivated people. Some investigators view these temperaments as attenuated forms of mood disorders that, while they may or may not cause significant impairment, still affect the patient's daily decisions and relationships. Patients often do not seek treatment for these symptoms and are not necessarily candidates for treatment, unless they express distress to the physician or the physician detects impairment in the patient's work life or interpersonal relationships. In that instance, psychiatric consultation should be sought, since an important question in treatment planning is the role of pharmacologic versus nonpharmacologic interventions.

**Table 5. Summary of DSM-IV-TR Criteria for Cyclothymic Disorder**

A. For at least 2 years, the presence of numerous periods with hypomanic symptoms and numerous periods with depressive symptoms that do not meet criteria for major depressive episode. Note: In children and adolescents, the duration must be at least 1 year.

B. During the above 2-year period (1 year in children and adolescents), the person has not been without the symptoms in Criterion A for more than 2 months at a time.

C. No major depressive episode, manic episode, or mixed episode has been present during the first 2 years of the disturbance. Note: After the initial 2 years (1 year in children and adolescents) of cyclothymic disorder, there may be superimposed manic or mixed episodes (in which case bipolar I disorder and cyclothymic disorder may be diagnosed ) or major depressive episodes (in which case bipolar II disorder and cyclothymic disorder may be diagnosed).

D. The symptoms in Criterion A are not better accounted for by schizoaffective disorder and are not superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or psychotic disorder, not otherwise specified.

E. The symptoms are not due to the direct physiologic effects of a substance (eg, a drug of abuse or medication) or a general medical condition (eg, hyperthyroidism).

F. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

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## Prevalence of Bipolar Disorders

Defining the spectrum of bipolar disorders has implications not only for treatment but also prevalence estimates. Although the lifetime prevalence of depression is very high (approximately 15%; Figure 1), BP-I, with clearly defined manic episodes, is less common, with lifetime prevalence estimated at approximately 1.6%, and the most recent epidemiologic study finds the combined prevalence of BP-I and BP-II to be 2.6%.[9,10]

Some investigators, who focus on bipolar spectrum disorders, also suggest that BP-I and especially BP-II may be underdiagnosed, and that the criteria for hypomania in DSM-IV are too strict. Angst and Cassano conducted a 20-year prospective community cohort study in Zurich ($n$ = 591) to measure the prevalence of bipolar spectrum disorders.[11] For BP-II, they compared the DSM-IV criteria to strict and broad versions of the Zurich criteria. The strict (or "hard") Zurich criteria, which are still more inclusive than DSM-IV, include euphoria, irritability, or overactivity, with at least 3 of the

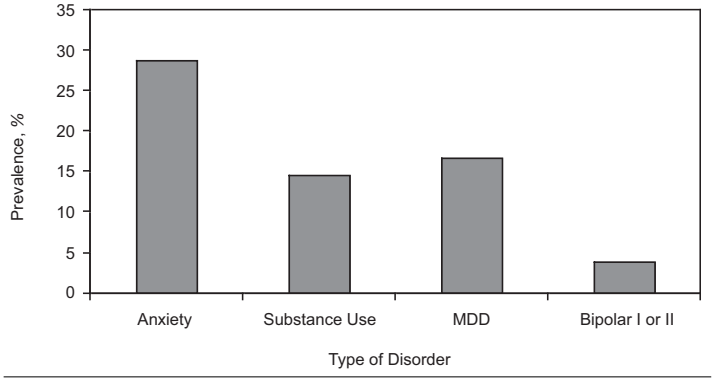
DSM-IV–defined symptoms of hypomania; experiencing symptoms for at least 1 day (whereas DSM-IV requires at least 4 days); and experiencing consequences of hypomania either by the patients themselves or received comments from others that something must be wrong with them. The broad (or "soft") criteria also require that patients have euphoria, irritability, or overactivity. However, patients have to present with only 2 of the 7 DSM-IV–defined symptoms of hypomania, and there is no minimum duration of hypomanic symptoms and no requirement for consequences resulting from the hypomania. As shown in Figure 2, the ratio of prevalence of MDD versus BP-I or BP-II varies dramatically (by almost an order of magnitude), depending on the crite-

**Table 6. Criteria for Affective Temperaments**

| Hyperthymic | Dysthymic | Cyclothymic | Irritable |
|---|---|---|---|
| Onset <21 years | Onset <21 years | Indeterminate early onset <21 years | Indeterminate early onset <21 years |
| Excessive use of denial | Given to worry | Intermittent short cycles with infrequent euthymia | Tendency to brood |
| Overinvolved and meddlesome | Quiet, passive, and indecisive | Hypersomnia alternating with decreased need for sleep | Hypercritical and complaining |
| Overconfident, self-assured, boastful | Self-critical, self-reproaching, and self-derogatory | Episodic promiscuity; repeated conjugal or romantic failure | Ill-humored joking |
| Intermittent subsyndromal hypomanic features with infrequent intervening euthymia | Skeptical, hypercritical, or complaining | Decreased verbal output alternating with talkativeness | Habitually moody, irritable, and choleric, with infrequent euthymia |
| Overtalkative and jocular | Intermittent low-grade depression not secondary to a nonaffective condition | Lethargy alternating with eutonia | Dysphoric restlessness |
| Cheerful, overoptimistic, or exuberant | Gloomy, pessimistic, humorless, or incapable of fun | Pessimism and brooding alternating with optimism and carefree attitudes | Impulsive |
| Warm, people-seeking, extraverted | Conscientious or self-disciplining | Frequent shift in work, study, interest, or future plans | Obtrusiveness |
| High energy level and full of improvident activities | Habitual hypersomnolence (9 hours/day) | Unexplained tearfulness alternating with excessive punning and jocularity | Does not meet criteria for antisocial personality, residual attention deficit disorder, or seizure disorder |
| Uninhibited, stimulus seeking, or promiscuous | Tendency to brooding, anhedonia, and psychomotor inertia (all worse in the morning) | Shaky self-esteem that alternates between lack of self-confidence and naïve or grandiose overconfidence | |
| Habitual short sleeper (<6 hours/day, including weekends) | Preoccupied with inadequacy, failure, and negativity to the point of morbid enjoyment of one's failure | Periods of mental confusion and apathy alternating with periods of sharpened and creative thinking | |
| | | Marked unevenness in quantity and quality of productivity associated with unusual working hours | |
| | | Uninhibited people seeking (hypersexuality may result) alternating with introverted self-absorption | |
| | | Biphasic illness characterized by abrupt shifts from 1 phase to the other and manifested subjectively and behaviorally | |

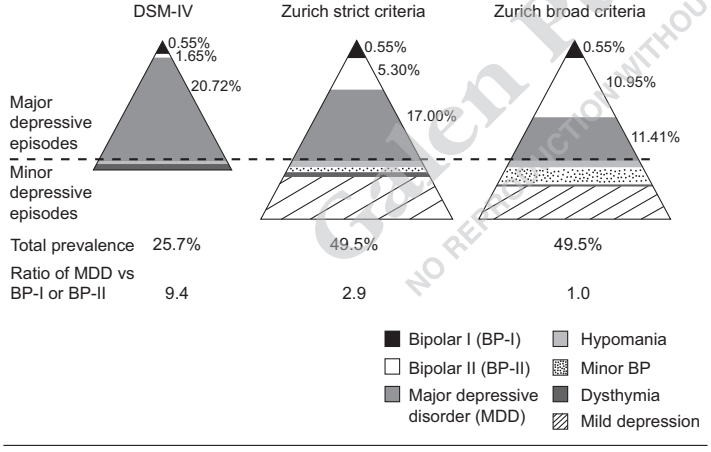
Adapted with permission from Akiskal and Mallya. *Psychopharmacol Bull.* 1987;23:68-73.[7]; Manning et al. *Arch Fam Med.* 1998;7:63-71.[8]

## Figure 1. Lifetime Prevalence of Major Psychiatric Disorders




Data are from a nationally representative face-to-face household survey conducted between February 2001 and April 2003 using the fully structured World Health Organization World Mental Health Survey version of the Composite International Diagnostic Interview.
*n* = 9282, age 18 years or older.
MDD = major depressive disorder.
Data from Kessler et al.[10]

## Figure 2. Broad Versus Narrow Criteria for Hypomania




The narrow (or hard) definition of hypomania had no minimum duration for hypomanic symptoms, and the patient had to show the following: suffering from euphoria or irritability or overactivity, have themselves experienced problems or received comments from others that something must be wrong with them, and present at least 3 of the 7 DSM-IV symptoms of hypomania.
The broad (or soft) definition of hypomania was defined as "any hypomanic symptoms" with no minimum duration. Also, the stem criteria and the element of consequences (ie, symptoms being noticed by others) were relaxed.
DSM-IV = *The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.*
Data from Angst et al.[2]
Reprinted with permission from Angst and Cassano. *Bipolar Disord.* 2005;7(suppl 4):4-12.[11]

ria used for bipolar disorder. The prevalence of BP-II could range from 1.65% (using DSM-IV criteria) to 10.95% using the broad Zurich criteria; using the broad criteria, many patients who meet criteria for MDD (ie, unipolar depression) in DSM-IV are instead diagnosed as having BP-II (Figure 2). Angst and Cassano justify the use of the broad criteria, which remain controversial, by noting that patients meeting broad criteria for hypomania are as likely to have a family history of BP as are patients meeting DSM-IV criteria for BP.[2-11]

Misdiagnosis remains a common problem. Studies of patients in family practice as well as psychiatric care settings suggest that 26% to 49% of patients being treated for a MDD have an unrecognized bipolar disorder.[12-15] Several other large studies have shown that most patients with bipolar disorder are initially misdiagnosed, most often with MDD, but also with anxiety or schizophrenia. For example, in 2000, a survey of support group participants diagnosed with bipolar disorder (*n* = 600) showed that most of the patients (69%) had been misdiagnosed initially. They had received a mean of 3.5 alternative diagnoses and seen a mean of 4 physicians before being diagnosed accurately. The most common incorrect diagnosis was MDD (60% of cases); others included anxiety disorder (26%), schizophrenia (18%), and borderline or antisocial personality disorder (17%). Also disturbing was the length of time between initial presentation for treatment and correct diagnosis. Thirty-eight percent reported a lapse of 10 or more years. Another 27% had waited from 1 to 5 years for the correct diagnosis.[16]

Recently, Das et al reported the results of systematic screening for bipolar disorder in an urban general medicine clinic serving a low-income population.[15] Of the 1157 patients screened, 9.8% were positive for a bipolar disorder (95% confidence interval, 8.0%–11.5%). Of those patients who screened positive, 72.3% had sought professional help but only 8.4% reported receiving a diagnosis of bipolar disorder. The other diagnoses were depression (79.5%) or anxiety/"bad nerves" or "nervous breakdown" (76.8%); the diagnoses were not mutually exclusive.[15] Prevalence studies therefore indicate that patients with bipolar disorder are frequently misdiagnosed in primary care settings.

### Distinguishing Bipolar from Unipolar Depression

Typically, patients with bipolar disorder experience far more depressive episodes than they do hypomanic

or manic episodes, and 35% to 60% of bipolar patients experience a major depressive episode before experiencing a manic episode.[17] In the 2005 study by Das et al, 49% of those who screened positive for bipolar disorder had evidence of current depression.[15] Epidemiologic studies indicate that the lifetime prevalence of mania or hypomania is only 1% to 2%, whereas that of major depressive episode is approximately 16.6%, thus screening for a bipolar disorder amongst patients presenting with depression may be akin to finding a needle in the haystack.[10] However, physicians should attempt to rule out bipolar disorder because of treatment implications (in patients with bipolar disorder, antidepressants are relatively contraindicated in the absence of mood stabilizers), morbidity (overall, bipolar disorder is a more severe impairing illness than unipolar depression, with more severe and frequent episodes leading to marital disruption, job loss, social problems, and financial stress), and mortality (increased risk of suicide).[4]

Importantly, one diagnoses depression in the context of bipolar disorder using the same criteria as for unipolar depression (ie, using the DSM-IV criteria for MDD; Table 4).[1] This highlights the fact that it is extremely difficult to differentiate unipolar depression from bipolar depression on the basis of clinical features alone, and that the ultimate differentiation of unipolar depressive disorder from bipolar disorder in a patient presenting with depressive symptoms rests on a careful assessment of past manic or hypomanic symptoms, along with focused questioning about family history. However, researchers have attempted to identify characteristic features of bipolar, as compared to unipolar, depression, in order to potentially decrease the possibility of bipolar depression being misdiagnosed as unipolar depression. Although there are no pathognomonic features of bipolar versus unipolar depression, there are subtle differences in clinical presentation that should increase one's suspicion of a bipolar disorder (Table 7).[8,18,19] These features should be considered in the context of a history of possible manic symptoms.

Indeed, the physician should always ask about past and present manic symptoms (possibly using the Mood Disorder Questionnaire [MDQ]), in addition to family history of bipolar disorder, in patients presenting with depression, anxiety, or other psychiatric symptoms, particularly if those symptoms are severe or impairing. In inquiring about family history, it is important to note that many family members with bipolar disorder may never have actually received the diagnosis. Therefore, it is important to ask about family history of suicide, substance abuse accompanied by mood swings, and other behaviors characteristic of a bipolar presentation. Finally, the presence in a depressed patient of any of the features noted in Table 7 should increase the physician's index of suspicion even further.[8,18,19] In screening for mania and depression, it is important for the physician to remember that mood disorders are not just about mood; there are associated physical and cognitive symptoms that occur at the same time. This is evident in the diagnostic criteria for mania (Table 1), hypomania (Table 2), and major depression (Table 4).[1]

### Eliciting History of Manic Symptoms

Although manic symptoms are, by definition, pathognomonic for bipolar disorder, they are much less frequently seen in the clinical setting, particularly in primary care. When patients present with depressive symptoms, many physicians do not think to look for past or present (hypo)manic symptoms and patients will most likely not offer this information spontaneously, or may focus solely on the somatic symptoms that are associated with either depression or mania. However, every depressed patient and every patient with a history of depression should be screened for possible bipolar disorder.[4] In addition, given the fact

**Table 7. Features That May Distinguish Bipolar from Unipolar Depression**

| |
|---|
| Sudden onset of episodes |
| Early age of onset of episodes |
| Recurrent episodes |
| Presence of mood-congruent psychosis (ie, the content of the patient's delusions or hallucinations is consistent with depressive themes: death, disease, guilt, nihilism, personal inadequacy, or punishment that is deserved) |
| Presence of psychomotor retardation, hypersomnia, and increased appetite or weight |
| Family history of bipolar disorder, especially loaded pedigrees, and lithium responsiveness to a mood disorder |
| High rates of substance abuse |

Data from Manning et al[8]; Glick[18]; Swann et al.[19]

that many patients with bipolar disorder also suffer from anxiety or substance abuse disorders, patients presenting with any one of these 3 illnesses should be screened for the presence of the other 2. Epidemiologic data show the high comorbidity rates of anxiety and substance use disorders with bipolar disorder. For example, the National Comorbidity Survey revealed that 95.5% of the study's patients with BP-I met criteria for 3 additional disorders, the most common of which were anxiety, substance use, and conduct disorders.[9] Boylan et al, in a survey of 138 patients with bipolar disorder who presented consecutively to a mental health clinic, showed that 55.8% of the patients had at least 1 comorbid anxiety disorder and 31.8% had 2 or more anxiety disorder diagnoses.[20]

The best available tool for detecting manic symptoms in a primary care setting is the MDQ, developed by Hirschfeld et al (Figure 3).[4,21] It is a simple questionnaire that can be completed by patients in just a few minutes. The MDQ addresses all of the characteristics of bipolar disorder: periodicity, mood, uncharacteristic behavior, and impairment. It was originally tested in psychiatric patients, for whom the sensitivity and specificity were both high (73% and 90%, respectively).[21] In community samples, the sensitivity is only 38% but specificity remains high (97%).[22] Several studies have shown that use of the MDQ increases detection of bipolar illness in primary care settings.[15,22]

Although the MDQ does not diagnose (hypo)mania, it is an effective screening tool. Nonetheless, one can argue that the MDQ could underdiagnose BP-II because it inquires about moderate to severe impairment and many patients view hypomanic episodes as periods of high functionality.[9] Thus, the onus rests on the clinician to probe for the symptoms of a manic or hypomanic episode via not only inquiries about the symptoms per se, but also about the consequences of such symptoms. These could include recurrent interpersonal conflicts, extreme extroversion that leads to interpersonal problems, legal problems, sexual promiscuity (or other behavior related to episodic impulsivity), sudden or frequent job or career changes, or severe and/or recurrent financial reverses or indiscretions.[19] Sleep hygiene is often a good indicator of manic



**Figure 3. The Mood Disorder Questionnaire**

| | Yes | No |
|---|---|---|
| 1. Has there ever been a period of time when you were not your usual self and … | | |
| You felt so good or so hyper that other people thought you were not your normal self or you were so hyper that you got into trouble? | ❒ | ❒ |
| You were so irritable that you shouted at people or started fights or arguments? | ❒ | ❒ |
| You felt much more self-confident than usual? | ❒ | ❒ |
| You got much less sleep than usual and found you didn't really miss it? | ❒ | ❒ |
| You were much more talkative or spoke much faster than usual? | ❒ | ❒ |
| Thoughts raced through your head or you couldn't slow your mind down? | ❒ | ❒ |
| You were so easily distracted by things around you that you had trouble concentrating or staying on track? | ❒ | ❒ |
| You had much more energy than usual? | ❒ | ❒ |
| You were much more active or did many more things than usual? | ❒ | ❒ |
| You were much more social or outgoing than usual; for example, you telephoned friends in the middle of the night? | ❒ | ❒ |
| You were much more interested in sex than usual? | ❒ | ❒ |
| You did things that were unusual for you or that other people might have thought were excessive, foolish, or risky? | ❒ | ❒ |
| Spending money got you or your family into trouble? | ❒ | ❒ |
| 2. If you checked YES to more than one of the above, have several of these ever happened during the same period of time? | ❒ | ❒ |
| 3. How much of a problem did any of these cause you—like being unable to work; having family, money, or legal troubles; or getting into arguments or fights? Please circle one response only. | | |
| No problem Minor problem Moderate problem Serious problem | | |
| 4. Have any of your blood relatives (ie, children, siblings, parents, grandparents, aunts, or uncles) had manic depressive illness or bipolar disorder? | ❒ | ❒ |
| 5. Has a health professional ever told you that you have manic-depressive illness or bipolar disorder? | ❒ | ❒ |

This instrument is designed for screening purposes only and is not to be used as a diagnostic tool.
Reprinted with permission from Kaye. *J Am Board Fam Pract.* 2005;18:271-281.[4] Courtesy of the University of Texas Medical Branch.

or hypomanic symptoms. If patients report requiring few hours of sleep, ask the patient if they are tired or napped the next day, what they did while they were awake (eg, worked or were productive, or did something that they later regretted). Also, if symptoms are endorsed on the MDQ, look for relatively discrete episodes of this behavior, and ask if others noticed the behavior. Thus, the clinician should ask for specific details and consequences of any manic or hypomanic symptoms and consider them in the context of the patient's lifestyle and history (ie, whether it is out of character).

## Conclusions

Some primary care physicians may never feel comfortable diagnosing a bipolar disorder. In any cases of doubt, the patient should be referred to a psychiatrist for a full evaluation. However, because of the current structure of our healthcare system (ie, separation of psychiatry from general medicine) and the societal stigma attached to some psychiatric illnesses, a referral to a psychiatrist may never be followed through. The diagnosis and management of a patient with a bipolar disorder then may come to rest on the shoulders of the primary care physician. Differentiating bipolar depression from unipolar depression is essential because of the treatment implications and severe morbidity and mortality sometimes associated with a bipolar disorder. Diagnosing bipolar disorder in primary care is possible and perhaps more importantly, screening for bipolar disorder may be best done in a primary care setting, in which a comprehensive and longitudinal relationship with the patient is more likely. In any patient with depressive symptoms, the primary care physician should inquire about past and present symptoms of (hypo)mania, inquire about a family history of bipolar disorder, recognize the depressive symptoms that are common in bipolar depression, and realize that mood disorders are about mood and physical and cognitive health.

## Discussion

### *Current Views of Bipolar Disorder*

***Dr Adams:*** People don't usually present to primary care saying, "I have bipolar disorder." Bipolar disorder is still strongly associated with a stigma; it's not something they want to have. The stigma is somewhat less now with anxiety, panic, possibly OCD (obsessive compulsive disorder), definitely depression. Therefore, they'll present to primary care and say, "I have depression." Bipolar disorder patients are perceived by patients in general as the people that kill their children and commit suicide, so you have to tread very lightly when you are going to talk about that diagnosis.

### *Screening for Bipolar Disorder*

***Dr Adams:*** Most primary care doctors are very hesitant to make the diagnosis of bipolar disorder. Dr Leibenluft said that the psychiatric diagnosis needs to be reliable, and in primary care it's often perceived that there is no quick, reliable way to make a diagnosis of bipolar disorder, or probably even depression. In my practice, we've integrated the MDQ into our depression template with our electronic medical records, and I recommend that everyone does that. I've been in private practice for approximately 15 years with a true interest in treating mental health disorders, although I treat all medical problems. There is a high comorbidity between mental health disorders, such as depression, anxiety, and ADD (attention deficit disorder). Therefore, I recommend using screening tools as early as possible, such as the Zung, MDQ, Connors rating scale, and many more.

The other issue in primary care is that we don't have to make the diagnosis at the first visit; psychiatrists do. Therefore, I can see someone, evaluate them, do a physical, run some blood tests, and bring them back and tell them what I think is going on.

***Dr Moore:*** That's essential, because the real challenge in primary care is that you don't have an hour or even 30 minutes; you've got 15 minutes. Patients are coming to the doctor with another complaint they want you to deal with, thus their mood may not even be on their agenda. I think the only way that we can really tackle this issue is using a tool like the MDQ. The unfortunate reality, though, is that there's often not physician continuity even in primary care. If someone is fortunate enough to be in a long-term relationship with a primary care doctor, then the potential for diagnosis is better, but the reality is patients often come into a large practice and see a different doctor every time.

***Dr Adams:*** I'm fortunate to have a very consistent patient population for 15 years, and that definitely is optimal.

***Dr Moore:*** Thus, there seems to be a compelling argument that in primary care we should give people an MDQ when we initially make a diagnosis of depression, and perhaps anxiety. We should perhaps

also give it to the patient again after 6 weeks of treatment, when they've shown improvement, to ensure that they're not now hypomanic. What are the other situations where we should think of screening for bipolar disorder and administering an MDQ?

***Dr Leibenluft:*** Besides depression and anxiety, substance abuse disorder and personality disorder patients should complete the MDQ. Detecting a personality disorder requires the longitudinal patient history, and this can be tricky. We also don't want to incorrectly identify those people as having bipolar disorder, but, on the other hand, if they are showing other signs (eg, lots of mood swings along with multiple marriages and multiple times of bankruptcies), the MDQ can be helpful.

***Dr Kaye:*** I would add postpartum-onset depression, first episode to your list of when to screen for bipolar disorder. That's very significant. Seasonality is another characteristic that can suggest bipolar disorder. The data aren't that strong for seasonality, but I find it helpful to use it as a clinical index of suspicion for a primary care physician.

***Dr Moore:*** In the primary care setting, the sensitivity of the MDQ is approximately 50% if the patient has depression, less if they don't. What else can we use to help us?

***Dr Leibenluft:*** The MDQ only asks about the DSM criteria for mania. It doesn't cover anything about life pattern, which can be very important. Therefore, the best thing is to get a psychiatric consultation, but sometimes you have to take a calculated risk. If you decide to medicate the patient, you want to go low and slow and do careful monitoring. Those are important issues: do you treat, and how do you treat?

### *The Symptom of Irritability*

***Dr Kaye:*** It seems that so much of what we see on television today (ie, commercials, docudramas, and crime-based TV shows) shows that virtually everyone who is irritable and moody is self-diagnosed as bipolar. You noted that in children it is one of the DSM-IV criteria for depression and mania, but not in adults.

***Dr Leibenluft:*** You raise an extremely important question. It goes back to the issues of boundaries for diagnosis-boundaries between what we would consider normal versus pathologic. Irritability is a very difficult symptom to assess when you've only got the patient in front of you and no secondary sources, because irritability is a symptom that often bothers the family and friends as much as it bothers the patient. On a practical level, it's important to look for impairment. In other words, you have to ask the patient, "Have you had arguments at work and lost a job, or didn't get a promotion, or got demoted, because of your mood? Have you gotten into physical fights?" With the symptoms of bipolar disorder, getting concrete examples is best. So, when someone says, "I'm irritable," you're interviewing for the consequences of the irritability (ie, have other people noticed it?). You take vague, common terms (eg, happy and irritable) and turn them into behaviors or consequences or lifetime contexts.

***Dr Ostacher:*** There's certainly an overlap with irritability between unipolar depression and bipolar disorder. In the DSM-IV, if the patient has irritability, they also need 4 associated symptoms and mood elevation to meet the criteria for a manic episode. If you're going to use irritability for diagnostic criteria, you have to make sure that the patient actually meets the other criteria for a manic episode in order to diagnose bipolar disorder. Nonetheless, irritability is really impairing for people, whether they have unipolar depression, bipolar disorder, or a substance use problem. It's something that is important to address in whatever psychiatric disorder the patient has.

***Dr Adams:*** In my family practice, I'll see people who have been married 3 or 4 times, had unfinished degrees, and can't hold a job.

***Dr Leibenluft:*** One of the important aspects of interviewing is that you have to get some part of the patient's life story to know those kinds of things. To make the diagnosis of bipolar disorder, you not only have to have the cross-sectional DSM-IV criteria, you also have to get some of the longitudinal life story. Physicians can develop the ability to relatively rapidly get a longitudinal life story, if they're practiced at it.

***Dr Ostacher:*** You can use the MDQ to look for mood elevation, but it doesn't ask about the duration of symptoms as part of the screening. It asks whether you have had these symptoms and whether you've had several together. It doesn't try to diagnose bipolar disorder. If you're doing an interview in which you want to use an episode as diagnostic of having bipolar disorder, you have to have all the symptoms in that episode. So you can't just have irritability and racing thoughts for 2 weeks. You have to have the irritability, racing thoughts, psychomotor agitation, impulsivity, and another symptom in order to meet the criteria. The screen is important, because it raises the question,

but then you still need to be more rigorous about whether people are having those symptoms during a single period of time.

***Dr Leibenluft:*** Actually, the specificity of the MDQ is much better than the sensitivity.

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