Recognition and Diagnosis of Bipolar Disorder

Robert M. A. Hirschfeld, M.D., and Lana A. Vornik, M.Sc.

Bipolar disorder is a serious, recurrent, and sometimes chronic psychiatric illness that is far more prevalent than many physicians realize. It often is unrecognized and misdiagnosed, particularly in patients presenting with depression. The consequences of misdiagnosis and mistreatment as unipolar depression may be disastrous. The rate of recognition may be improved by asking patients about bipolar symptoms and by screening for bipolar disorder using the Mood Disorder Questionnaire.

(J Clin Psychiatry 2004;65[suppl 15]:5–9)

Bipolar disorder is a serious, recurrent, and occasionally chronic psychiatric disease. Bipolar disorder is characterized by a dysregulation of mood and associated impulsivity, risky behavior (e.g., alcohol abuse, sexual indiscretion, excessive spending), and interpersonal problems. Because of these problems, individuals with bipolar disorder experience increased mortality from suicide, natural causes (e.g., cardiovascular disease), homicide, and accidents.[1–4] Recent data suggest that bipolar disorder is third only to depression and schizophrenia among psychiatric disorders in the loss of healthy life due to premature death or disability.[5]

Bipolar I disorder has been the focus of most research on bipolar disorder. A diagnosis of bipolar I requires at least 1 episode of mania, defined as a week or longer period of abnormally elevated or irritable mood with associated symptoms, such as decreased need for sleep, more talkative than usual, racing thoughts, and excessive involvement in high-risk activities.[6] A manic episode causes a marked impairment in social or occupational functioning and often requires hospitalization.

The lifetime prevalence rate of bipolar I disorder is approximately 1%,[7] as diagnosed by the criteria of the *Diagnostic and Statistical Manual of Mental Disorders*, Third Edition, Text Revision. In the United States, the lifetime prevalence rates for bipolar I disorder were reported to be 0.8% in the Epidemiological Catchment Area study[8] and 1.6% in the National Comorbidity Survey.[9]

Bipolar disorder, however, encompasses a much broader range of illness than bipolar I disorder. This range of illness often is referred to as bipolar spectrum disorder[10–12] and includes bipolar I disorder, bipolar II disorder, and other forms of bipolar disorder. In 1992, Young and Klerman[13] proposed inclusion of 6 different clinical states, including those with unipolar depression in families heavily loaded with bipolar disorder (Table 1). More recently, Akiskal and Pinto[14] proposed a bipolar spectrum with 7 subtypes, including masked bipolarity and hyperthymic depression (Table 2).

Bipolar spectrum disorder is a longitudinal diagnosis involving abnormal mood swings, including mania, hypomania, mixed states, hyperthymic temperament, major depressive episode, and depressive mixed states. Mania is a persistent elevation of mood with accompanying symptoms and severe psychosocial impairment.[6] Hypomania is similar to mania, but less severe. In mixed states, criteria for both mania and major depressive episodes (except for duration) are met for nearly every day during at least a 1-week period. Depressive mixed states are characterized by unrelenting dysphoria and irritability, extreme fatigue, racing thoughts, anxiety and panic attacks, and suicidal obsessions and impulses.[15] Hyperthymic temperament includes attributes that constitute a part of the long-term functioning of the individual. Individuals with hyperthymic temperament generally are thought of as extremely outgoing and ambitious.[15,16] Such individuals often are quite successful in business and sales, although their grandiose and risk-taking attitudes may at times cause serious legal, financial, or interpersonal problems.

Many authorities[10,11,17] have suggested that these milder forms of bipolar disorder are more frequent than bipolar I disorder. Lifetime prevalence rates for bipolar spectrum disorder have been reported to range from 3.0% to 6.5%

From the University of Texas Medical Branch, Galveston.

Based in part on a presentation at the National Summit Meeting of the Bipolar Care OPTIONS initiative, which was held September 4–6, 2003, in Washington, D.C., and supported by an unrestricted educational grant from Janssen Medical Affairs, L.L.C.

Corresponding author and reprints: Robert M. A. Hirschfeld, M.D., Dept. of Psychiatry and Behavioral Sciences, University of Texas Medical Branch, 301 University Blvd., Galveston, TX 77555-0188.

Table 1. Proposal of 6 Subtypes of Bipolar Spectrum Disorder[a]

Types	Characteristics
Bipolar I	Depression with full-blown mania
Bipolar II	Hypomania and depression
Bipolar III	Hypomania and depressive symptoms
Bipolar IV	Secondary to disease or drugs
Bipolar V	Major depression with a family history of bipolar disorder
Bipolar VI	Unipolar mania

[a]From Hirschfeld,[12] based on Young and Klerman.[13]

Table 2: Proposal of 7 Subtypes of Bipolar Spectrum Disorder[a]

Types	Characteristics
Bipolar I	Depression with full-blown mania
Bipolar I ½	Depression with protracted hypomania
Bipolar II	Depression with hypomania
Bipolar II ½	Cyclothymic depression
Bipolar III	Antidepressant-associated hypomania
Bipolar III ½	Bipolarity masked—and unmasked—by stimulant abuse
Bipolar IV	Hyperthymic depression

[a]From Hirschfeld,[12] adapted from Akiskal and Pinto.[14]

Table 3. Lifetime Prevalence Rates of Bipolar Spectrum Disorder[a]

Study	Instrument	Prevalence	Rate (%)
Weissman and Myers (1978)	SADS-L	Lifetime	3.0
Oliver and Simmons (1985)	DIS	Lifetime	3.3
Faravelli and Incerpi (1985)	SI	1 year	3.4
Heun and Maier (1993)	SADS-L	Lifetime	6.5
Levav et al (1993)	SADS-L	6 months	2.6
Angst (1995)	SPIKE	Lifetime	5.5
Szadoczky et al (1998)	CIDI	Lifetime	5.1

[a]Reprinted with permission from Angst.[17]
Abbreviations: CIDI = Composite International Diagnostic Interview, DIS = Diagnostic Interview Schedule, SADS-L = Schedule for Affective Disorders and Schizophrenia-Lifetime Version, SI = structured interview, SPIKE = semistructured interview.

Table 4. Steps to Avoid Misdiagnosis of Unipolar Depression in Bipolar Patients Initially Presenting With Depressive Symptoms

Steps
Ask about a history of mania or hypomania
Ask about family history of bipolar disorder
Involve family members or significant others in the evaluation process
Administer a screening instrument for bipolar disorder, the Mood Disorder Questionnaire

across 7 studies (Table 3).[17] However, most of these studies were small and used varying definitions of bipolar spectrum disorder.[17] No prospective large-scale epidemiologic study has examined the prevalence of bipolar spectrum disorder in adults using DSM-IV criteria.

The problems of misdiagnosis and underdiagnosis of bipolar spectrum disorder have been highlighted recently.[11,12] Correct diagnosis is essential, because the treatment for bipolar disorder differs significantly from the treatment for major depressive disorder. There is a risk of inducing mania in patients with bipolar spectrum disorder who are treated solely with antidepressant agents.[11,18,19]

DIAGNOSIS OF BIPOLAR SPECTRUM DISORDER

Most patients with bipolar spectrum disorder seek treatment for depression, rather than for mania or hypomania. In a recent survey of its members, the Depression and Bipolar Support Alliance (formerly the National Depressive and Manic-Depressive Association [NDMDA]) found that 60% of its members with bipolar spectrum disorder sought treatment because of depression.[20] Other reasons included anxiety symptoms, difficulty sleeping, and substance abuse. Patients rarely present with hypomania. When they are manic, they often come to medical attention because of intervention by family or legal authorities.

Unfortunately, in their assessments of patients with depression, physicians often neglect to ask about a history of mood swings and mania. Consequently, the diagnosis of bipolar spectrum disorder often is missed. For example, in a study of 108 consecutive outpatients with depression or anxiety in a private family practice setting, 26% had a diagnosis of bipolar spectrum disorder, the majority of whom had bipolar II disorder, and only 1 of whom had been diagnosed previously. Another 15 bipolar II patients were identified in a semistructured interview in which patients recalled a history of hypomania.[21] In Italy, Perugi et al.[22] assessed 86 consecutive day-hospital patients and outpatients with DSM-IV major depressive episode with atypical features (i.e., mood reactivity, weight gain, hypersomnia, leaden paralysis, and rejection sensitivity). They found that 72% of these patients had bipolar spectrum disorder, and that more than half of those patients had bipolar II disorder. This represented one third of the depressed group. In a recent study of patients seen in an outpatient clinic over the course of 1 year, 37% experienced a manic or hypomanic episode, but were misdiagnosed as having unipolar depression.[23]

Consequences of Misdiagnosis

Mistreatment of bipolar disorder as unipolar depression can trigger manic episodes or otherwise destabilize the illness in patients with bipolar disorder. In a study of patients with bipolar disorder who previously had been mistreated for unipolar depression, 55% developed mania or hypomania, and 23% developed new or accelerated rapid cycling.[23] Certain steps should be taken by the clinician to avoid misdiagnosis of unipolar depression in patients with bipolar disorder (Table 4).

This lack of recognition and attention to the possibility of bipolar spectrum disorder leads to substantial delay in patients receiving an accurate diagnosis. In a survey of its members completed in the early 1990s,[24] the NDMDA found that nearly one quarter of patients consulted a pro-

fessional within 6 months of onset of their symptoms. However, 48% of patients consulted 3 or more professionals before receiving a correct diagnosis, and 10% consulted 7 or more professionals before correctly being identified as having bipolar disorder. Thirty-four percent of patients waited 10 years or more for their first diagnosis of bipolar disorder. In another sample of bipolar patients entering the Stanley Foundation Bipolar Treatment Outcome Network,[25] the mean length of time to first treatment of bipolar disorder was 10 years. In the most recent NDMDA survey, the results were nearly identical: 34% of NDMDA members reported waiting 10 years or more for their first accurate diagnosis of bipolar disorder.[20]

Clinical Course

Patients with bipolar disorder in general remain true to their diagnosis over time. In a 10-year follow-up of patients in the National Institute of Mental Health Collaborative Program on the Psychobiology of Depression,[26] two thirds (66%) of patients with bipolar I disorder had a manic episode during the follow-up period, whereas only 7.5% of bipolar II patients had a manic episode in that period. More than one third (34%) of bipolar II patients had at least 1 hypomanic episode. Among those who had a diagnosis of nonbipolar depression at index, only 5% had a hypomanic episode and just 5.2% had a manic episode during a 10-year follow-up.[26]

Judd et al.[27] conducted a prospective follow-up of patients with bipolar I disorder. The patients were followed for at least 2 years for a mean of 12.8 years of follow-up. Patients with bipolar I disorder were symptomatically ill 47.3% of the time. Depressive symptoms accounted for 67% of the time that the patients were ill, pure mania accounted for 20%, and mixed states accounted for 13%. Depression (but not mania) predicted greater future illness burden and chronicity.

SCREENING FOR BIPOLAR DISORDER: THE MOOD DISORDER QUESTIONNAIRE

Screening for bipolar disorder can be extremely helpful, especially among patients receiving antidepressant treatment. A brief and easy-to-use screening instrument for bipolar spectrum disorder, the Mood Disorder Questionnaire (MDQ), recently has been developed and tested.[28] The MDQ is a self-report, single-page, paper-and-pencil inventory that can be scored quickly and easily by a physician, nurse, or any trained medical staff assistant. The MDQ screens for lifetime history of manic or hypomanic syndrome by asking 13 yes/no items derived from the DSM-IV criteria and from clinical experience (Appendix 1). An additional yes/no question asks whether several of any reported manic or hypomanic symptoms or behaviors were experienced concurrently. Finally, the level of functional impairment due to these symptoms also is assessed.

The MDQ in the Clinic

The MDQ was validated in a study conducted at 5 outpatient psychiatric clinics with special expertise in mood disorders.[28] After providing informed consent, patients filled out the MDQ. A random subsample of these patients received a research diagnostic interview (the Structured Clinical Interview for DSM-IV [SCID]) by telephone within 2 weeks by a trained interviewer to obtain a diagnosis of bipolar spectrum disorder (including bipolar I, bipolar II, and bipolar disorder not otherwise specified). The interviewer was blind to the clinical diagnosis of the patient and to the MDQ results. A group of 198 patients received the telephone diagnostic interview, of whom 63% were female, and the mean age was 44 years. Fifty-five percent of the patients received a research (SCID) diagnosis of bipolar disorder.

A cutoff point of 7 or more was selected for a positive screen, which provided good sensitivity (0.73, 95% CI = 0.65 to 0.81) and very good specificity (0.90, 95% CI = 0.84 to 0.96). By using this threshold, 7 of 10 people with bipolar spectrum disorder would be correctly identified by the MDQ, and 9 of 10 people who do not have bipolar disorder would be accurately screened out.

The MDQ in the Community

The MDQ was tested as a screen for bipolar disorder in the general community.[29] The MDQ was mailed to 100,000 demographically representative U.S. households. A supplemental mailing was sent to 27,800 individuals who were selected to improve the representative nature of the combined samples for matching adults aged 18 years or older. The household sample was balanced to match census data for U.S. households for the 9 geographic census regions, household size and income, and age of head of household within each census region for market size. Nearly 72% (71,836) of the household questionnaires were returned within 6 weeks, and 17,973 (64.7%) questionnaires from the individual-based sample were returned within 5 weeks. The final data set included 85,358 (66.8%) usable returns for analysis. The prevalence of bipolar disorder as measured by the MDQ was 3.7%.[29]

A validity study was conducted using a subsample (N = 695) of these subjects, who also received telephone interviews involving an abbreviated version of the SCID. It was determined that in the general population, sensitivity and specificity of the MDQ were 0.28 and 0.97, respectively.[30]

Health Care Professional Diagnosis of Bipolar Disorder

Of the individuals with positive MDQ screens in the nationwide community study,[29] only 19.8% reported that they previously had received a diagnosis of bipolar disorder from a doctor. A larger percentage (31.2%) of those who screened positive reported a physician diagnosis of

unipolar depression. An additional 49.0% reported no diagnosis of either bipolar disorder or unipolar depression. Of those who screened negative, 1.4% reported a physician diagnosis of bipolar disorder, and 9.5% reported a diagnosis of unipolar depression.[29]

Impact of Bipolar Disorder on People's Lives

Several substudies[31–34] of the nationwide community study[29] investigated the impact of bipolar spectrum disorder on people's lives. Those individuals with positive MDQ screens were significantly more affected by their symptoms than were those with negative screens. Subjects with positive screens experienced more days of disruptive symptoms, were at risk for more work and relationship problems, and had more medical comorbidities than did subjects with negative MDQ screens. One study[33] compared the impact of depressive symptoms versus manic symptoms in patients with bipolar disorder. Depressive symptoms were more frequent than manic symptoms, and depressive symptoms were more likely to disrupt work as well as social and family life functioning than manic symptoms. Bipolar depressed patients experienced significantly worse depressive symptoms than did unipolar depressed patients. Bipolar depressed patients were more likely to report being impaired all or most of the time in their ability to do work than were unipolar depressed patients.

CONCLUSION

Bipolar disorder is a pernicious illness that is far more prevalent than many clinicians appreciate. It often is unrecognized and misdiagnosed, particularly in depressed people. The consequences of misdiagnosis and mistreatment as unipolar depression may be disastrous. The rate of recognition may be improved by asking about bipolar symptoms during evaluations and by screening for bipolar disorder using the MDQ. The MDQ can be accessed on the web site of the Depression and Bipolar Support Alliance (www.dbsalliance.org), as well as on the web sites of several pharmaceutical companies. The MDQ has been translated into a number of languages, including Spanish, French, German, Portuguese, Japanese, Finnish, and Estonian.

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Appendix 1. The Mood Disorder Questionnaire[a]

Instructions: This questionnaire is an important part of providing you with the best health care possible. Your answers will help in understanding problems that you may have. Please answer each question as best you can.

	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; getting into arguments or fights? *Please circle one response only.*

No problem Minor problem Moderate problem Serious problem

	YES	NO
4. Have any of your blood relatives (i.e. children, siblings, parents, grandparents, aunts, 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?	❑	❑

THANK YOU FOR COMPLETING THIS QUESTIONNAIRE. PLEASE RETURN THIS FORM TO YOUR DOCTOR.

[a]Reprinted with permission from Hirschfeld et al.[28]