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CME Objective

After studying the article by Zimmerman et al, you should be able to:

 Use differences in demographic, clinical, and family history variables when distinguishing bipolar disorder from major depressive disorder with comorbid borderline personality disorder

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Distinguishing Bipolar II Depression From Major Depressive Disorder With Comorbid Borderline Personality Disorder: Demographic, Clinical, and Family History Differences

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ABSTRACT

Objective: Because of the potential treatment implications, it is clinically important to distinguish between bipolar II depression and major depressive disorder with comorbid borderline personality disorder. The high frequency of diagnostic co-occurrence and resemblance of phenomenological features has led some authors to suggest that borderline personality disorder is part of the bipolar spectrum. Few studies have directly compared patients with bipolar disorder and borderline personality disorder. In the present study from the Rhode Island Methods to Improve Diagnostic Assessment and Services project, we compared these 2 groups of patients on demographic, clinical, and family history variables.

Method: From December 1995 to May 2012, 3,600 psychiatric patients presenting to the outpatient practice at Rhode Island Hospital (Providence, Rhode Island) were evaluated with semistructured diagnostic interviews for DSM-IV Axis I and Axis II disorders. The focus of the present study is the 206 patients with DSM-IV major depressive disorder and borderline personality disorder (MDD-BPD) and 62 patients with DSM-IV bipolar II depression without borderline personality disorder.

Results: The patients with MDD-BPD were significantly more often diagnosed with posttraumatic stress disorder (P<.001), a current substance use disorder (P<.01), somatoform disorder (P<.05), and other nonborderline personality disorder (P<.05). Clinical ratings of anger, anxiety, paranoid ideation, and somatization were significantly higher in the MDD-BPD group (all P<.01). The MDD-BPD patients were rated significantly lower on the Global Assessment of Functioning (P<.001), their current social functioning was poorer (P<.01), and they made significantly more suicide attempts (P<.01). The patients with bipolar II depression had a significantly higher morbid risk for bipolar disorder in their first-degree relatives than the MDD-BPD patients (P<.05).

Conclusions: Patients diagnosed with bipolar II depression and major depressive disorder with comorbid borderline personality disorder differed on a number of clinical and family history variables, thereby supporting the validity of this distinction.

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- Because of the potential treatment implications, it is clinically important to recognize both bipolar disorder and borderline personality disorder in patients seeking treatment for depression, and it is important to distinguish between the two.
- Compared to bipolar II depressed patients, patients with major depressive disorder and borderline personality disorder (MDD-BPD) had more comorbid psychiatric disorders; greater severity of anger, anxiety, paranoid ideation, and somatization; poorer social functioning; and more suicide attempts. The patients with bipolar II depression had a significantly higher morbid risk for bipolar disorder in their first-degree relatives than the MDD-BPD patients.
- The findings of the study support the validity of distinguishing between bipolar II disorder and borderline personality disorder.

epression is a significant public health problem, with the Global Burden of Disease study predicting that by the year 2020 depression will be the second leading cause of death and disability worldwide. However, depression is a heterogeneous condition. Some patients who meet symptom criteria for a major depressive episode have bipolar disorder.

The underrecognition of bipolar disorder has been identified as a significant clinical problem.^{2–5} For patients diagnosed with bipolar disorder, the lag between initial treatment seeking and the correct diagnosis is often more than 10 years.⁶ The treatment and clinical implications of the failure to recognize bipolar disorder in depressed patients include the underprescription of mood-stabilizing medications, an increased risk of rapid cycling, and increased costs of care.^{3,7,8} As a result, experts have called for improved recognition of bipolar disorder,^{2,4} and screening scales have been developed and recommended to facilitate the identification of bipolar disorder.^{9,10}

Borderline personality disorder (BPD) is a common comorbidity in depressed patients that is also underdiagnosed. Compared to patients with major depressive disorder (MDD) without BPD, patients with MDD and BPD (MDD-BPD) also have excess psychosocial morbidity. 12,13 The recognition of BPD is clinically important because of the availability of specific psychotherapies that are effective 14–16 and the possible overprescription of medications that have little benefit, carry the risk of medically significant side effects, 17,18 and might even worsen outcome. 19

Because of the potential treatment implications, it is clinically important to recognize both bipolar disorder and BPD in patients seeking treatment for depression, and it is important to distinguish between the two. However, diagnostic confusion sometimes exists between the 2 disorders. ^{20–22} Such confusion would be expected, because the 2 disorders share some phenomenological features. Given the superficial resemblance of some of the clinical characteristics of bipolar disorder and BPD, it is not surprising that the 2 disorders frequently co-occur. ²¹

The relatively high frequency of diagnostic co-occurrence and resemblance of phenomenological features have led some authors to suggest that BPD is part of the bipolar spectrum. ^{23,24} In fact, in a recent large-scale international study, ⁵ BPD comorbidity was considered as one of the variables validating the distinction between bipolar and nonbipolar disorder. Several review articles ^{21,22,25,26} have summarized the evidence in support of and opposition to the hypothesis that BPD belongs to the bipolar spectrum. One of the noteworthy findings of these review articles is that few studies have directly compared individuals diagnosed with bipolar disorder and BPD. Moreover, the few studies that have directly compared the 2 disorders have been based on small samples and examined a limited number of variables.

Atre-Vaidya and Hussain²⁷ compared 10 patients with BPD to 13 patients with bipolar disorder on the Temperament and Character Inventory and found significant differences on 3 of 7 personality dimensions. Berrocal and colleagues²⁸ compared 25 BPD patients without a current or lifetime history of mood disorders, 16 patients with bipolar disorder without BPD, and 19 patients with MDD without BPD on a self-report measure of lifetime mood phenomenology and found no significant differences between those with BPD and those with bipolar disorder. Henry et al²⁹ compared 4 groups of patients: BPD without bipolar II disorder (n = 29), bipolar II without BPD (n = 14), BPD and bipolar II (n = 12), and a control group of patients who did not meet criteria for either disorder but had another personality disorder (n = 93). They found that both BPD and bipolar II disorder were associated with increased levels of affective lability, although the specific nature of such lability differed. BPD was associated with greater degrees of impulsiveness and hostility compared to patients without BPD. Their analysis, however, did not directly compare the BPD and bipolar II groups, but instead was a 2-way analysis of variance with the presence or absence of BPD and bipolar II as the main factors; thus, the significant differences were largely due to differences with patients who had neither of the 2 disorders. Wilson et al³⁰ likewise compared 4 groups of patients, BPD with MDD (n = 72), bipolar II depressed without BPD (n = 15), BPD and bipolar II depressed (n=15), and a control group of patients with MDD without BPD (n = 71), on measures of impulsiveness, hostility, and depression symptom severity. Patients with BPD reported significantly higher levels of impulsiveness, hostility, and cognitive and anxious symptoms. The statistical analytic approach was similar to the one used by Henry et al²⁹ in that the authors did not directly compare the BPD and bipolar II groups, but instead used a 2-way analysis of variance with the presence or absence of BPD and bipolar II as the factors; thus, the significant differences may have been largely due to differences with the MDD-only group. Perry and Cooper³¹ compared 10 patients with BPD and 9 with bipolar II disorder on types of psychodynamic conflicts and found several differences, although no differences were found in the type of defense mechanisms used. Finally, Nilsson et al³² compared female outpatients with bipolar I disorder (n=25) and BPD (n=31) who were in remission

from an affective episode and found that the patients with BPD scored significantly higher on the cyclothymic, depressive, irritable, and anxious temperament subscales of the Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego Autoquestionnaire, whereas the patients with bipolar disorder scored higher on the hyperthermic subscale. The patients with BPD also scored higher on 14 of 18 indices of maladaptive self-schemas. While these studies have been limited by small sample sizes and a small number of variables, they have been consistent in finding symptom and personality trait profiles distinguishing BPD from bipolar disorder.

We are not aware of any study that has focused on depressed patients presenting for treatment and comparing those who are diagnosed with either bipolar II disorder or BPD—a clinically important distinction faced by clinicians. The goal of the present study from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project was to directly compare these 2 groups of patients to identify variables that would assist clinicians in making this differential diagnosis. We hypothesized that patients with bipolar II depression would have a greater family history of bipolar disorder, and that depressed patients with borderline personality disorder would have higher prevalences of childhood trauma, diagnoses of posttraumatic stress disorder, and other personality pathology and poorer levels of social functioning.

METHOD

The Rhode Island MIDAS project represents an integration of research methodology into a community-based outpatient practice affiliated with an academic medical center and has been described previously.³³ The institutional review committee of Rhode Island Hospital (Providence, Rhode Island) approved the research protocol, and all patients provided informed, written consent.

The sample examined in the present report is derived from the 3,600 psychiatric outpatients evaluated with semistructured diagnostic interviews from December 1995 to May 2012, 206 of whom were diagnosed with major depressive disorder with borderline personality disorder (MDD-BPD), 92 of whom were diagnosed with bipolar II disorder, and all 298 of whom met criteria for a major depressive episode at the time of presentation. Patients whose depressive episode was in partial or full remission were excluded. Patients were interviewed by a diagnostic rater who administered a modified version of the Structured Clinical Interview for DSM-IV (SCID)³⁴ and the BPD section of the Structured Interview for DSM-IV Personality (SIDP-IV). 35 The SCID was supplemented with questions from the Schedule for Affective Disorders and Schizophrenia (SADS)³⁶ on best level of social functioning during the past 5 years, the amount of time unemployed during the past 5 years, and symptom severity ratings of anxiety, anger, somatization, and paranoid ideation. During the course of the MIDAS project, the assessment battery has been modified at times. The assessment of all DSM-IV personality disorders was not introduced until the study was well underway and the procedural details of incorporating research interviews into our clinical practice had been well established, although we had introduced the assessment of borderline and antisocial personality disorder near the beginning of the study. In June 2008, we stopped administering the full SIDP-IV and continued to administer the BPD module only. The assessment of personality disorders always followed the assessment of Axis I disorders. Information on BPD was missing for 4 patients with bipolar II disorder, and these patients were excluded from the analysis. We also excluded the 26 patients diagnosed with both BPD and bipolar II disorder. This left a final sample of 62 patients with bipolar II depression and 206 with MDD-BPD.

The 268 patients included 80 men (29.9%) and 188 women (70.1%) who ranged in age from 18 to 68 years (mean [SD] = 33.9 [10.4] years). About one-third of the subjects were married (29.5%, n=79); the remainder were single (41.8%, n=112), divorced (14.9%, n=40), separated (4.9%, n=13), widowed (0.4%, n=1), or living with someone as if in a marital relationship (8.6%, n=23). Approximately two-thirds of the patients attended school beyond high school (75.4%, n=202), although only a minority graduated a 4-year college (16.4%, n=44). The racial composition of the sample was 86.9% (n=233) white, 6.0% (n=16) black, 4.1% (n=11) Hispanic, 0.8% (n=2) Asian, and 2.2% (n=6) from another racial background or a combination of the above racial backgrounds.

Following the SCID, patients completed a booklet of questionnaires that included the Childhood Trauma Questionnaire.³⁷ We compared the groups on the 5 subscales of the Childhood Trauma Questionnaire—emotional abuse, physical abuse, sexual abuse, physical neglect, and emotional neglect.

All patients were rated using the Clinical Global Impression (CGI) of depression severity³⁸ and Global Assessment of Functioning (GAF). Family history diagnoses were based on information provided by the patient. The interview followed the guide provided in the Family History Research Diagnostic Criteria³⁹ and assessed the presence or absence of problems with anxiety, mood, substance use, and other psychiatric disorders for all first-degree family members. Information about functional impairment, types of treatment, and hospitalizations of the family members was also recorded. Morbid risks were calculated using agecorrected denominators or bezugsiffers based on Weinberg's shorter method. 40 Thus, relatives over the age of risk for the particular illness were given a value of 1, those within the age for risk were given a value of 0.5, and those below it were given a value of 0. These ages of risk were based on the distribution of ages at onset in our probands. 41 Morbid risks were compared using the χ^2 statistic.

The diagnostic raters were highly trained and monitored throughout the project to minimize rater drift as has been described in prior reports from the MIDAS project. ³³ Reliability was examined in 65 patients. Of relevance to the present report, the reliabilities for diagnosing MDD (κ =0.90) and bipolar disorder (κ =0.75) were good. The reliability for diagnosing BPD (κ =1.0) was excellent.

Data Analysis

We compared the demographic, family history, and clinical characteristics of patients with MDD-BPD and patients with bipolar II disorder who met criteria for a major depressive episode at the time of the evaluation. t Tests were used to compare the groups on continuously distributed variables. Categorical variables were compared by the χ^2 statistic, or by Fisher exact test if the expected value in any cell of a 2×2 table was less than 5.

RESULTS

The MDD-BPD group was significantly younger (mean [SD] age of 33.0 [9.7] vs 36.9 [12.1] years, t = 2.3, P < .05) and less likely to be married (25.2% vs 43.5%, χ^2 = 7.7, P < .01) than the bipolar II disorder group. There was no difference in race, education level, or gender.

The total number of current Axis I disorders was significantly higher in the MDD-BPD patients than the patients with bipolar II depression (mean [SD] of 2.7 [1.6] vs 1.8 [1.3], t=3.9, P<.001), and significantly more patients with MDD-BPD were diagnosed with 3 or more current Axis I disorders (Table 1). The majority of both groups had a current anxiety disorder, although the rate of any anxiety disorder was significantly higher in the patients with MDD-BPD (Table 1). Posttraumatic stress disorder was the only specific anxiety disorder that was significantly more frequent in the MDD-BPD group. The patients with MDD-BPD were significantly more often diagnosed with a current substance use disorder, somatoform disorder, and other nonborderline personality disorder (Table 1). Because of the low rates of individual personality disorder diagnoses, we also examined personality disorder dimensional scores. We calculated a dimensional score for each DSM-IV personality disorder based on the number of criteria that were present. The MDD-BPD group had significantly higher scores on the paranoid, schizotypal, antisocial, histrionic, narcissistic, dependent, and obsessive-compulsive personality disorder dimensions (Table 2).

There were several symptom differences between the 2 groups. On the SCID, the MDD-BPD patients significantly more often reported depressed mood, worthlessness, psychomotor retardation, death wishes, and suicidal thoughts at the time of the evaluation (Table 3). The MDD-BPD patients were rated higher on the SADS items evaluating level of anger, anxiety, paranoid ideation, and somatization (Table 4). No symptom was more frequent or rated more highly in the patients with bipolar II depression. The mean age at onset of the first major depressive episode was below 20 years and not significantly different in the 2 groups. The duration of the current episode was significantly longer in the MDD-BPD group, and the MDD-BPD group was rated as significantly more severely depressed on the CGI (Table 4).

The MDD-BPD patients were rated significantly lower on the GAF, and their current social functioning was poorer (Table 5). A significantly greater number of patients in the MDD-BPD group were rated 50 or lower on the GAF (77.6%)

Table 1. Frequency of Current *DSM-IV* Axis I and Axis II Disorders in Depressed Outpatients With Bipolar II Depression (n=62) and Major Depressive Disorder With Borderline Personality Disorder (MDD-BPD; n=206)

		Bipolar II		MDD-BPD		
Disorder	n	%	n	%	χ^2	P
Anxiety disorders						
Panic with or without	15	24.2	67	32.5	1.6	NS
agoraphobia						
Specific phobia	8	12.9	46	22.3	2.6	NS
Social phobia	25	40.3	101	49.0	1.4	NS
Posttraumatic stress disorder	6	9.7	62	30.1	10.5	<.001
Obsessive-compulsive disorder	5	8.1	27	13.1	1.2	NS
Generalized anxiety disorder	20	32.3	66	32.0	0.0	NS
Any anxiety disorder	45	72.6	180	87.4	7.8	<.01
Substance use disorders						
Alcohol abuse/dependence	3	4.8	40	19.4	7.5	< .01
Drug abuse/dependence	3	4.8	22	10.7	1.9	NS
Any substance use disorder	6	9.7	52	25.2	6.8	< .01
Any eating disorder	9	14.5	30	14.6	0.0	NS
Any somatoform disorder	4	6.5	35	17.0	4.3	< .05
Any impulse-control disorder	3	4.8	5	2.4	1.0	NS
Three or more Axis I disorders	16	25.8	103	38.4	11.3	<.001
Personality disorders ^a						
Paranoid	1	2.6	23	19.2	6.3	<.01
Schizoid	0	0.0	1	0.8	0.3	NS
Schizotypal	0	0.0	3	2.5	1.0	NS
Antisocial	1	2.6	10	8.3	1.5	NS
Histrionic	1	2.6	2	1.7	0.1	NS
Narcissistic	1	2.6	6	5.0	0.4	NS
Avoidant	9	23.1	34	28.3	0.4	NS
Dependent	2	5.1	12	10.0	0.9	NS
Obsessive-compulsive	2	5.1	12	10.0	0.9	NS
Any personality disorder	15	38.5	68	56.7	3.9	< .05
Two or more personality	1	2.6	25	20.8	7.2	<.01
disorders						

^aThe assessment of all *DSM-IV* personality disorders was conducted in 39 patients with bipolar II disorder and 120 with MDD-BPD.

Table 2. DSM-IV Personality Disorder Dimensional Scores in Depressed Outpatients With Bipolar II Depression (n = 39) and Major Depressive Disorder With Borderline Personality Disorder (MDD-BPD; n = 120)

	Bipolar II		MDD-	MDD-BPD		
Personality Disorder	Mean	SD	Mean	SD	t	P
Paranoid	0.7	1.1	1.9	1.7	4.8	<.001
Schizoid	0.6	0.8	0.7	0.9	0.5	NS
Schizotypal	0.4	0.7	1.0	1.3	3.5	.001
Antisocial	0.3	0.8	1.2	1.5	4.2	<.001
Histrionic	0.8	1.3	1.4	1.4	2.2	< .05
Narcissistic	0.9	1.4	1.7	1.6	2.8	<.01
Avoidant	1.9	2.4	2.3	2.3	1.0	NS
Dependent	0.6	1.3	1.8	1.8	4.5	<.001
Obsessive-compulsive	1.2	1.1	1.8	1.3	2.7	< .01

vs 56.5%, χ^2 = 10.7, P<.001) and as having poor current social functioning (46.6% vs 32.3%, χ^2 = 4.0, P<.05). The 2 groups did not differ in the lifetime number of psychiatric hospitalizations or the amount of time missed from work during the past 5 years due to psychiatric reasons (Table 5). The MDD-BPD patients made significantly more suicide attempts (Table 5), and twice as many patients with MDD-BPD than bipolar II depression had made 3 or more prior suicide attempts, although the difference was not significant (13.6% vs 6.5%, χ^2 = 2.3, NS).

The patients with bipolar II depression had a significantly higher morbid risk for bipolar disorder in their first-

Table 3. Frequency of Depressive Symptoms in Depressed Outpatients With Bipolar II Depression (n = 62) and Major Depressive Disorder With Borderline Personality Disorder (MDD-BPD; n = 206)

	Bip	Bipolar II		MDD-BPD		
Symptom	n	%	n	%	χ^2	P
Depressed mood	51	82.3	196	95.1	11.0	<.001
Loss of interest or pleasure	45	72.6	170	82.5	3.0	NS
Appetite/weight disturbance						
Decreased appetite	22	35.5	90	43.7	1.3	NS
Increased appetite	15	24.2	51	24.8	0.0	NS
Decreased weight	13	21.0	54	26.2	0.7	NS
Increased weight	13	21.0	38	18.4	0.2	NS
Sleep disturbance						
Insomnia	42	67.7	136	66.0	0.1	NS
Hypersomnia	13	21.0	44	21.4	0.0	NS
Psychomotor change						
Psychomotor agitation	19	30.6	74	35.9	0.6	NS
Psychomotor retardation	6	9.7	52	25.2	6.8	<.01
Loss of energy	49	79.0	170	82.5	0.4	NS
Worthlessness/excessive guilt						
Worthlessness	35	56.5	157	76.2	9.2	< .01
Excessive guilt	32	51.6	134	65.0	3.6	NS
Concentration/indecision						
Diminished concentration	46	74.2	171	83.0	2.4	NS
Indecisiveness	35	56.5	119	57.8	0.3	NS
Death/suicidal thoughts						
Thoughts of death	30	48.4	136	66.0	6.3	<.01
Suicidal ideas, plan, or attempt	15	24.2	81	39.3	4.7	<.05

Table 4. Clinical Characteristics of Depression in Depressed Outpatients With *DSM-IV* Bipolar II Depression (n = 62) and Major Depressive Disorder With Borderline Personality Disorder (MDD-BPD; n = 206)

	Bipolar II		MDD-BPD			
Clinical Characteristic	Mean	SD	Mean	SD	t	P
Age at onset of depression, y	18.2	10.1	17.1	9.1	-0.8	NS
No. of depressive episodes	25.5	37.7	10.6	26.0	-2.9	< .01
Current episode duration, wk	101.5	191.9	356.8	539.7	5.7	<.001
Clinical Global Impression of	3.1	0.5	3.3	0.6	3.0	< .01
depression severity						
Subjectively experienced anger ^a	2.2	1.6	3.4	1.3	5.2	< .001
Expressed anger ^a	1.2	1.3	2.4	1.4	5.8	< .001
Psychic anxiety ^a	2.6	1.6	2.9	1.5	1.4	NS
Somatic anxiety ^a	2.0	1.5	2.7	1.5	2.8	< .01
Somatization ^a	0.4	1.0	0.9	1.4	3.1	<.01
Paranoid ideation ^a	1.2	1.4	1.9	1.3	3.9	< .001

^aBased on the Schedule for Affective Disorders and Schizophrenia.

Table 5. Psychosocial Morbidity in Depressed Outpatients With Bipolar II Depression (n=62) and Major Depressive Disorder With Borderline Personality Disorder (MDD-BPD; n=206)

	Bipolar II		MDD-BPD			
Morbidity Indicator	Mean	SD	Mean	SD	t	P
Global Assessment of Functioning	49.4	6.4	45.2	8.9	-3.5	<.001
No. of psychiatric hospitalizations	0.8	1.5	1.2	5.6	0.5	NS
No. of suicide attempts	0.6	1.3	1.6	4.3	2.8	< .01
Current social functioning	3.0	1.2	3.6	1.3	3.0	<.01
(past 5 y) ^a						
Adolescent social functioning (12–18 y) ^a	3.1	1.0	3.2	1.1	0.5	NS
Time unemployed in past 5 y ^b	3.3	2.3	3.5	2.3	0.6	NS

^aBased on the Schedule for Affective Disorders and Schizophrenia.
^bExpressed as a rating on the applicable Schedule for Affective Disorders and Schizophrenia item. Patients who were not expected to work (eg, student, retired) were excluded, leaving a final sample of 56 with bipolar II disorder and 188 with MDD-BPD.

degree relatives than the MDD-BPD group (5.9% vs 3.0%, χ^2 = 3.9, P<.05). The MDD-BPD group scored significantly higher on the physical neglect subscale of the Childhood Trauma Questionnaire (mean [SD] score of 14.2 [5.8] vs 11.6 [4.4], t = 3.1, P<.01). Scores on the other subscales of the Childhood Trauma Questionnaire were also higher in the MDD-BPD patients, but none of these differences were significant.

DISCUSSION

The current study is the largest and most extensive comparison of patients presenting for outpatient treatment of a major depressive episode who were diagnosed with bipolar II disorder or comorbid BPD. Compared to depressed patients with bipolar II disorder, the depressed patients with BPD had poorer social functioning, higher rates of posttraumatic stress disorder and substance use disorders at the time of the evaluation, and more suicidal ideation; made more suicide attempts; and were more angry, paranoid, and somatic. These findings support the validity of distinguishing between bipolar II disorder and BPD.

A number of researchers have suggested that BPD belongs on the bipolar spectrum. 5,23,24 We have noted elsewhere that the variables used to validate the bipolar spectrum overlap with the variables used to validate BPD.⁴² There are relatively few disorder-specific validators. We would propose that 5 disorder-specific validators are type of affective lability, temperament, childhood trauma history, comorbid posttraumatic stress disorder, and family history of bipolar disorder. Prior studies have found that, compared to those with bipolar disorder, patients with BPD experience more affective lability characterized by irritability. ^{29,30,32} While we did not include a measure of affective switches in the present study, we found that during the week before the evaluation the patients with BPD reported higher levels of subjective and overtly expressed anger. We did not include a measure of temperament, although other studies have found temperamental differences between these 2 diagnostic groups.^{27,32} We found that posttraumatic stress disorder was significantly more often diagnosed in the patients with BPD. The difference between groups on the Childhood Trauma Questionnaire was not as great as the difference in rates of trauma-related diagnoses. A family history of bipolar disorder was greater in the first-degree family members of the bipolar II probands.

In the present study, we used the *DSM-IV* definition of bipolar II disorder, which requires a minimum duration of 4 days to diagnose a hypomanic episode. Some researchers advocate a broader definition of bipolar disorder that requires only a 1- or 2-day duration to define hypomania. ^{43,44} On the basis of *DSM-IV*'s narrower definition, we found that MDD-BPD was approximately 3 times more frequent than bipolar II disorder. The relative prevalence of these 2 disorders

would obviously change if the definition of bipolar II disorder were broadened. We also predict that greater diagnostic confusion and diagnostic error would occur if a broader definition of bipolar II disorder were used. It is likely that the transient periods of affective instability characterized by anger and irritability that are typical of borderline personality disorder would be more often misinterpreted as indicative of a hypomanic episode. Consequently, broadening the definition of bipolar II disorder would result in more false-positive bipolar II diagnoses, and the diagnostic groups would not be as clearly distinguished.

During the past few years, our clinical-research group has identified a problem with the overdiagnosis of bipolar disorder that is at least as frequent as the problem with underdiagnosis. 45 BPD was frequently diagnosed in patients who were overdiagnosed with bipolar disorder. 46 Some authors have been critical of our assertions about the overdiagnosis of bipolar disorder. 47 However, the critique fails to acknowledge that we validated our findings regarding overdiagnosis with family history information. That is, the morbid risk of bipolar disorder in the patients we considered to have been overdiagnosed with bipolar disorder was significantly lower than the morbid risk of bipolar disorder in patients whom we diagnosed with bipolar disorder and no different than the morbid risk of bipolar disorder in patients who were never diagnosed with bipolar disorder. Likewise, we found that the morbid risk of bipolar disorder in patients with MDD-BPD was no different than in patients with MDD without BPD and lower than in patients with bipolar disorder. 42 The results of the present study extend our prior findings and support the validity of distinguishing between bipolar disorder and BPD.

A limitation of the study was that it was conducted in a single outpatient practice in which the majority of patients were white, were female, and had health insurance. Replication of the results in samples with different demographic characteristics is warranted. While the study was of psychiatric outpatients, approximately one-quarter of the patients had been previously hospitalized. We focused on patients who were depressed at the time of the evaluation. The depressed state could have biased the assessment of some variables such as personality disorders. However, this bias should have been similar across diagnostic groups. We focused on patients who were in a depressive episode at the time of the evaluation because it would have been more difficult to interpret some of findings based on symptom differences, level of psychosocial functioning, and personality variables if we included patients who were in various stages of symptom remission. Moreover, there is research support of the validity of personality disorder assessment in depressed patients.⁴⁸ The assessment of episode duration and number of prior episodes was based on retrospective recall. A longitudinal prospective follow-up study with repeated assessments would better clarify the persistence of depressive symptoms and syndromes in these 2 groups. We did not include a third group of depressed patients, those diagnosed with MDD who did not have BPD, because we wanted to focus on the 2 groups that are

sometimes difficult to differentiate. Elsewhere, we compared depressed patients with and without comorbid BPD.⁴²

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents that is outside US Food and Drug Administration—approved labeling has been presented in this article.

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REFERENCES

- Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: Global Burden of Disease Study. *Lancet*. 1997;349(9064):1498–1504.
- Bowden CL. Strategies to reduce misdiagnosis of bipolar depression. Psychiatr Serv. 2001;52(1):51–55.
- Ghaemi SN, Boiman EE, Goodwin FK. Diagnosing bipolar disorder and the effect of antidepressants: a naturalistic study. J Clin Psychiatry. 2000;61(10): 804–808, quiz 809.
- 4. Hirschfeld RM. Bipolar spectrum disorder: improving its recognition and diagnosis. *J Clin Psychiatry*. 2001;62(suppl 14):5–9.
- Angst J, Azorin JM, Bowden CL, et a; BRIDGE Study Group. Prevalence and characteristics of undiagnosed bipolar disorders in patients with a major depressive episode: the BRIDGE study. Arch Gen Psychiatry. 2011;68(8): 791–798.
- Hirschfeld RM, Lewis L, Vornik LA. Perceptions and impact of bipolar disorder: how far have we really come? results of the National Depressive and Manic-Depressive Association 2000 survey of individuals with bipolar disorder. J Clin Psychiatry. 2003;64(2):161–174.
- Birnbaum HG, Shi L, Dial E, et al. Economic consequences of not recognizing bipolar disorder patients: a cross-sectional descriptive analysis. *J Clin Psychiatry*. 2003;64(10):1201–1209.
- Matza LS, Rajagopalan KS, Thompson CL, et al. Misdiagnosed patients with bipolar disorder: comorbidities, treatment patterns, and direct treatment costs. *J Clin Psychiatry*. 2005;66(11):1432–1440.
- Hirschfeld RM, Williams JB, Spitzer RL, et al. Development and validation of a screening instrument for bipolar spectrum disorder: the Mood Disorder Questionnaire. Am J Psychiatry. 2000;157(11):1873–1875.
- Parker G, Fletcher K, Barrett M, et al. Screening for bipolar disorder: the utility and comparative properties of the MSS and MDQ measures. J Affect Disord. 2008;109(1–2):83–89.
- Zimmerman M, Mattia JI. Differences between clinical and research practices in diagnosing borderline personality disorder. Am J Psychiatry. 1999;156(10): 1570–1574.
- Bellino S, Patria L, Paradiso E, et al. Major depression in patients with borderline personality disorder: a clinical investigation. *Can J Psychiatry*. 2005;50(4):234–238.
- Joyce PR, Mulder RT, Luty SE, et al. Borderline personality disorder in major depression: symptomatology, temperament, character, differential drug response, and 6-month outcome. *Compr Psychiatry*. 2003;44(1):35–43.
- Bateman A, Fonagy P. Eight-year follow-up of patients treated for borderline personality disorder: mentalization-based treatment versus treatment as usual. *Am J Psychiatry*. 2008;165(5):631–638.
- Blum N, St John D, Pfohl B, et al. Systems Training for Emotional Predictability and Problem Solving (STEPPS) for outpatients with borderline personality disorder: a randomized controlled trial and 1-year follow-up. Am J Psychiatry. 2008;165(4):468–478.
- Kliem S, Kröger C, Kosfelder J. Dialectical behavior therapy for borderline personality disorder: a meta-analysis using mixed-effects modeling. J Consult Clin Psychol. 2010;78(6):936–951.
- Bender DS, Dolan RT, Skodol AE, et al. Treatment utilization by patients with personality disorders. Am J Psychiatry. 2001;158(2):295–302.
- Zanarini MC, Frankenburg FR, Hennen J, et al. Mental health service utilization by borderline personality disorder patients and Axis II comparison subjects followed prospectively for 6 years. J Clin Psychiatry. 2004;65(1):28–36.
- Gardner DL, Cowdry RW. Alprazolam-induced dyscontrol in borderline personality disorder. Am J Psychiatry. 1985;142(1):98–100.
- Zimmerman M, Galione JN, Ruggero CJ, et al. Screening for bipolar disorder and finding borderline personality disorder. J Clin Psychiatry. 2010;71(9):1212–1217.

- Paris J, Gunderson J, Weinberg I. The interface between borderline personality disorder and bipolar spectrum disorders. Compr Psychiatry. 2007;48(2):145–154.
- Magill CA. The boundary between borderline personality disorder and bipolar disorder: current concepts and challenges. *Can J Psychiatry*. 2004;49(8):551–556.
- Akiskal HS. Demystifying borderline personality: critique of the concept and unorthodox reflections on its natural kinship with the bipolar spectrum. Acta Psychiatr Scand. 2004;110(6):401–407.
- Pérugi G, Toni C, Travierso MC, et al. The role of cyclothymia in atypical depression: toward a data-based reconceptualization of the borderline-bipolar II connection. J Affect Disord. 2003;73(1–2):87–98.
- Paris J. Borderline or bipolar? distinguishing borderline personality disorder from bipolar spectrum disorders. Harv Rev Psychiatry. 2004;12(3):140–145.
- Smith DJ, Muir WJ, Blackwood DH. Is borderline personality disorder part of the bipolar spectrum? Harv Rev Psychiatry. 2004;12(3):133–139.
- 27. Atre-Vaidya N, Hussain SM. Borderline personality disorder and bipolar mood disorder: two distinct disorders or a continuum? *J Nerv Ment Dis.* 1999;187(5):313–315.
- Berrocal C, Ruiz Moreno MA, Rando MA, et al. Borderline personality disorder and mood spectrum. Psychiatry Res. 2008;159(3):300–307.
- Henry C, Mitropoulou V, New AS, et al. Affective instability and impulsivity in borderline personality and bipolar II disorders: similarities and differences. J Psychiatr Res. 2001;35(6):307–312.
- 30. Wilson ST, Stanley B, Oquendo MA, et al. Comparing impulsiveness, hostility, and depression in borderline personality disorder and bipolar II disorder. *J Clin Psychiatry*. 2007;68(10):1533–1539.
- Perry JC, Cooper SH. A preliminary report on defenses and conflicts associated with borderline personality disorder. J Am Psychoanal Assoc. 1986;34(4):863–893.
- Nilsson AK, Jørgensen CR, Straarup KN, et al. Severity of affective temperament and maladaptive self-schemas differentiate borderline patients, bipolar patients, and controls. Compr Psychiatry. 2010;51(5):486–491.
- 33. Zimmerman M. Integrating the assessment methods of researchers in routine clinical practice: The Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project. In: First M, ed. Standardized Evaluation in Clinical Practice. Washington, DC: American Psychiatric Publishing, Inc; 2003:29–74.
- 34. First MB, Spitzer RL, Gibbon M, et al. Structured Clinical Interview for

- DSM-IV Axis I Disorders-Patient Edition (SCID-I/P, version 2.0). New York, NY: Biometrics Research Department, New York State Psychiatric Institute; 1995.
- Pfohl B, Blum N, Zimmerman M. Structured Interview for DSM-IV Personality. Washington, DC: American Psychiatric Press, Inc.; 1997.
- Endicott J, Spitzer RL. A diagnostic interview: the schedule for affective disorders and schizophrenia. Arch Gen Psychiatry. 1978;35(7):837–844.
- Bernstein DP, Fink L, Handelsman L, et al. Initial reliability and validity of a new retrospective measure of child abuse and neglect. *Am J Psychiatry*. 1994;151(8):1132–1136.
- 38. Guy W. ECDEU Assessment Manual for Psychopharmacology. Rockville, MD: National Institute of Mental Health; 1976.
- Endicott J, Andreasen N, Spitzer RL. Family History Research Diagnostic Criteria. 3rd ed. New York, NY: Biometrics Research, New York State Psychiatric Institute; 1978.
- Stromgren E. Statistical and genetic population studies within psychiatry: methods and principal results. Actualities Scientifiques et Industrelles, 1101 Congres International de Psychiatrie. 1950;6:155–157.
- Zimmerman M, Chelminski I. Generalized anxiety disorder in patients with major depression: is *DSM-IV*'s hierarchy correct? *Am J Psychiatry*. 2003;160(3): 504–512.
- 42. Galione J, Zimmerman M. A comparison of depressed patients with and without borderline personality disorder: implications for interpreting studies of the validity of the bipolar spectrum. *J Pers Disord*. 2010;24(6):763–772.
- Angst J, Gamma A, Benazzi F, et al. Toward a re-definition of subthreshold bipolarity: epidemiology and proposed criteria for bipolar-II, minor bipolar disorders and hypomania. J Affect Disord. 2003;73(1–2):133–146.
- 44. Benazzi F. Testing predictors of bipolar-II disorder with a 2-day minimum duration of hypomania. *Psychiatry Res.* 2007;153(2):153–162.
- Zimmerman M, Ruggero CJ, Chelminski I, et al. Is bipolar disorder overdiagnosed? J Clin Psychiatry. 2008;69(6):935–940.
- Zimmerman M, Ruggero CJ, Chelminski I, et al. Psychiatric diagnoses in patients previously overdiagnosed with bipolar disorder. *J Clin Psychiatry*. 2010;71(1):26–31.
- 47. Phelps J, Ghaemi SN. The mistaken claim of bipolar "overdiagnosis": solving the false positives problem for *DSM-5/ICD-11*. *Acta Psychiatr Scand*. 2012;126(6):395–401.
- Morey LC, Shea MT, Markowitz JC, et al. State effects of major depression on the assessment of personality and personality disorder. Am J Psychiatry. 2010;167(5):528–535.



POSTTEST

To obtain credit, go to PSYCHIATRIST.COM (Keyword: September) to take this Posttest and complete the Evaluation online.

- 1. Which of the following symptoms of depression was significantly more common among patients in this study with major depressive disorder and comorbid borderline personality disorder (MDD-BPD) than among those with bipolar II depression?
 - a. Depressed mood
 - b. Increased appetite and weight
 - c. Sleeping too much or too little
 - d. Indecisiveness
- Which of the following clinical characteristics was significantly greater among patients in this study with bipolar II depression than among those with MDD-BPD?
 - a. Mean number of depressive episodes
 - b. Paranoid ideation
 - c. Expressed anger
 - d. Somatic anxiety

- 3. In the DSM-IV and DSM-5 definitions of bipolar II disorder, a minimum duration of 4 consecutive days is required to diagnose a hypomanic episode, in which the person has an abnormally and persistently elevated, expansive, or irritable mood and increased activity most of the day almost every day. While irritability or anger occurs in both bipolar II disorder and BPD, the irritability is more transient in BPD than in hypomania.
 - a. True
 - b. False
- 4. Ms A, who is 26 years old, had her first major depressive episode when she was 19 years old. She is presenting for treatment of another depressive episode. Ms A has no personal or family history of mania, but her mother also experienced depressive episodes. When you are confirming her diagnosis of MDD, what variable would suggest that you should consider a comorbid BPD diagnosis?
 - a. Her age at onset of MDD
 - b. Her history of 3 suicide attempts
 - c. Her time spent unemployed in the past 5 years
 - d. Her adolescent social functioning