

The relationship between borderline personality disorder and bipolar disorder

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It is clinically important to recognize both bipolar disorder and borderline personality disorder (BPD) in patients seeking treatment for depression, and it is important to distinguish between the two. Research considering whether BPD should be considered part of a bipolar spectrum reaches differing conclusions. We reviewed the most studied question on the relationship between BPD and bipolar disorder: their diagnostic concordance. Across studies, approximately 10% of patients with BPD had bipolar I disorder and another 10% had bipolar II disorder. Likewise, approximately 20% of bipolar II patients were diagnosed with BPD, though only 10% of bipolar I patients were diagnosed with BPD. While the comorbidity rates are substantial, each disorder is nonetheless diagnosed in the absence of the other in the vast majority of cases (80% to 90%). In studies examining personality disorders broadly, other personality disorders were more commonly diagnosed in bipolar patients than was BPD. Likewise, the converse is also true: other axis I disorders such as major depression, substance abuse, and post-traumatic stress disorder are also more commonly diagnosed in patients with BPD than is bipolar disorder. These findings challenge the notion that BPD is part of the bipolar spectrum.

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Introduction

The under-recognition of bipolar disorder in patients presenting for the treatment of depression has been identified as a significant clinical problem.¹⁻¹¹ The diagnosis of bipolar disorder is often delayed, with the time between initial treatment seeking and the correct diagnosis often taking more than 10 years.^{12,13} The treatment and clinical implications of the failure to recognize bipolar disorder in depressed patients are significant, and include the underprescription of mood-stabilizing medications, an increased risk of rapid cycling, and increased costs of care.^{4,14-16} As a result of the potential morbidity associated with a delay in diagnosis, experts have called for improved recognition of bipolar disorder,^{1,6} and screening scales have been developed and recommended to facilitate the identification of bipolar disorder.¹⁷⁻¹⁹

Borderline personality disorder (BPD) is a common comorbidity in depressed patients that is also underdiagnosed.²⁰ Compared with patients with major depressive disorder (MDD) without BPD, patients with MDD and BPD also have excess psychosocial morbidity.^{21,22} The recognition of BPD is clinically important because of the availability of specific psychotherapies that are

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effective^{23,24} and the possible overprescription of medications that have little benefit and carry the risk of medically significant side effects.²⁵

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, this presupposes that each is a valid diagnostic entity. During the past 20 years there have been increasing suggestions that BPD should be conceptualized as part of the spectrum of bipolar disorder. Advocates of the bipolar spectrum suggest that treatments that have been found effective in treating bipolar disorder should be used when treating patients with BPD because of its inclusion on the bipolar spectrum.^{6,26-28}

Literature reviews considering whether BPD belongs to the bipolar spectrum have reached differing conclusions. Smith et al²⁹ suggested that a strong case could be made that a significant percentage of patients with BPD fall into the bipolar spectrum, and Belli et al³⁰ concluded that the two disorders are closely linked in phenomenology and treatment response. Antoniadis et al³¹ and Coulston et al³² did not draw a conclusion regarding BPD's inclusion on the bipolar spectrum, whereas Paris et al³³ and Dolan-Sewell et al³⁴ concluded that empirical evidence did not support BPD's link to the bipolar spectrum. Sripada and Silk,³⁵ reviewing neuroimaging studies, noted that there were some areas of overlap and some differences between BPD and bipolar disorder. Some of the authors of these reviews noted that few studies have directly compared patients with bipolar disorder and BPD, and they called for such empirical data to help clarify the relationship between the two disorders.^{32,35}

In the present review we focus on the most studied question on the relationship between BPD and bipolar disorder—their diagnostic concordance. More than 30 studies have examined the frequency of bipolar disorder in patients with borderline personality disorder, or the frequency of BPD in patients with bipolar disorder. We address the following questions: (i) What is the frequency of each disorder when the other is present? (ii) Is the level of co-occurrence elevated? That is, is the prevalence of BPD significantly higher in patients with bipolar disorder than in other psychiatric disorders? (iii) Is BPD the most common personality disorder in bipolar patients or are other personality disorders more frequent?

Methodological issues in personality disorder assessment

Any review of a topic involving personality disorders needs to consider assessment methodology, because assessment issues can have a significant impact on the findings. In short, there should be some consideration of the who, what, and when of personality disorder assessment. To be sure, these are also issues in the evaluation of Axis I disorders, though they have not been studied as much as they have been studied in the personality disorder field.

Who should be questioned when assessing personality disorders—the target individual or someone who knows the target individual well? The evaluation of personality disorders presents special problems that may require the use of informants. In contrast to the symptoms of major Axis I disorders, the defining features of personality disorders are based on an extended longitudinal perspective of how individuals act in different situations, how they perceive and interact with a constantly changing environment, and the perceived reasonableness of their behaviors and cognitions. Only a minority of the personality disorder criteria are discrete, easily enumerated behaviors. For any individual to describe their normal personality they must be somewhat introspective and aware of the effect their attitudes and behaviors have on others. But insight is the very thing usually lacking in individuals with a personality disorder. *DSM-IV* notes that the characteristics defining a personality disorder may not be considered problematic by the affected individual (ie, ego-syntonic) and suggests that information be obtained from informants. Research comparing patient and informant report of personality pathology has found marked disagreement between the two sources of information.³⁶⁻³⁹ Only one of the studies examining the frequency of personality disorders in patients with bipolar disorder examined the impact of informant assessment on the rates of personality disorder diagnoses.⁴⁰ Peselow et al⁴⁰ presented personality disorder rates based on independent patient and informant interviews, and we have included in *Table 1* the results based on the patient information in order to be consistent with other studies.

What measures should be used to diagnose personality disorders? Several instruments exist, and while there is no evidence that any one interview schedule is more reliable or valid than another, there is consistent evidence that prevalence rates are higher based on self-administered scales than clinician interviews.⁴¹⁻⁴³

Author	Bipolar diagnostic measure	Bipolar diagnostic criteria	Borderline diagnostic measure	Borderline diagnostic criteria	Psychiatric status at time of evaluation	Sample
Alnaes ⁸⁰	SCID	DSM-III	SIDP	DSM-III	Symptomatic	Consecutive outpatients
Barbato ⁸⁵	Chart	DSM-III	IPDE	DSM-III	In remission	Patients receiving case management
Benazzi ⁷¹	SCID	DSM-IV	SCID	DSM-IV	In depressive episode	Consecutive outpatients
Benazzi ⁷²	SCID	DSM-IV	SCID	DSM-IV	In depressive episode	Consecutive outpatients
Brieger ⁸⁶	SCID	DSM-IV	SCID	DSM-IV	Largely in remission, shortly before discharge	Consecutive inpatients with mood symptoms
Carpenter ⁸⁷	NR	DSM-III-R	PDE	DSM-III-R	No-mild symptoms on the expanded BPRS	Married bipolar I outpatients
Carpiniello ⁷⁸	SCID	DSM-IV	SCID	DSM-IV	Stable clinical remission over the last month	Consecutive outpatients with lifetime bipolar I or bipolar II disorder
Comtois ⁸¹	SCID	DSM-III-R	SCID	DSM-III-R	Symptomatic	Consecutive outpatients
Dunayevich ⁸⁸	SCID	DSM-III-R	SCID	DSM-III-R	Near discharge when sufficiently improved	Consecutive bipolar I inpatients admitted for manic or mixed episode
Garno ⁷⁷	SCID	DSM-IV	SCID	DSM-IV	Nonsyndromal, though mean HAMD in Cluster B patients was 18.6	Consecutively derived from Bipolar Disorders Research Clinic, 95% outpatients, ¾ bipolar I
Gasperini ⁸⁹	DIS	DSM-III-R	SIDP	DSM-III-R	Normothymic	Patients in a lithium clinic for at least 2 years without co-existing axis I disorder
George ⁹⁰	SCID	DSM-III-R	PDE	DSM-III-R	In remission	Bipolar I patients participating in 2-year study with at least 1 caregiver willing to participate and no comorbid substance use disorder
Joyce ⁸²	SCID	DSM-IV	SCID	DSM-IV	In depressive episode	Depressed patients in medication treatment trial
Loftus ⁹¹	SCID	DSM-IV	SCID	DSM-IV	No-mild depressive or manic symptoms (≤ 17 on HAMD and ≤ 15 on CARSM)	Predominantly outpatients (47, 4 inpts) recruited into 2-year longitudinal study
Perugi ⁸³	SCID	DSM-III-R	SCID	DSM-III-R	Symptomatic	Outpatients (71%) and day hospital patients (29%) with atypical depression
Peselow ⁴⁰	SADS	RDC	SIDP	DSM-III	Assessed patients while hypomanic and euthymic	Outpatients initiating treatment for a hypomanic or manic episode
Pica ⁶³	SCID	DSM-III-R	SIDP	DSM-III-R	The patient was judged to be "settled"; Low symptom levels on scales	Inpatients with bipolar disorder (n=16) or schizoaffective disorder bipolar type (n=10).
Preston ¹²³	SCID	DSM-IV	SCID	DSM-IV	Evaluated 15 months after recruitment into drug study	Participants in drug study who were located 15 months after study. Patients with rapid cycling, substance abuse or PD severe enough to interfere with study were excluded.

Table I. Methods of studies of the frequency of borderline personality disorder in individuals with bipolar disorder. *DSM*, *Diagnostic and Statistical Manual for Mental Disorders*; SCID, Structured Clinical Interview for *DSM-IV* (or *DSM-III-R*); PDE, Personality Disorders Examination; IPDE, International Personality Disorders Examination; DIS, Diagnostic Interview Schedule; SIDP, Structured Interview for *DSM* Personality; HAMD, Hamilton Rating Scale for Depression; BPRS, Brief Psychiatric Rating Scale; SADS-L, Schedule for Affective Disorders and Schizophrenia Lifetime version; RDC, Research Diagnostic Criteria; CARSM, Clinician Administered Rating Scale for Mania

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When should personality disorders be assessed during the course of the mood disorder? The impact of psychiatric state on personality disorder assessment has been well established, and to minimize this effect some researchers evaluate personality disorders after a patient has improved and is in a euthymic state.⁴⁴⁻⁴⁶ The potential problem with this approach is that it underestimates the prevalence of personality disorders because the presence of personality pathology predicts poorer outcome. Therefore, we included all studies, regardless of when personality disorders were assessed, with the plan to examine the potential impact of psychiatric state on prevalence rates.

Excluded studies

To obtain a systematic and comprehensive collection of published studies of comorbidity, we conducted a Medline and PsycInfo search on the terms bipolar and borderline. We reviewed the titles from this search to identify studies that potentially included information on the comorbidity of bipolar disorder and BPD. We also identified studies in reference lists of identified studies and review articles.

Several studies that have been included in other reviews of bipolar disorder-BPD comorbidity were excluded from the present review. Self-report measures of personality disorders are more appropriately considered screening instruments than diagnostic measures. Consistent with this, as noted above, prevalence rates based on self-report scales are higher than those based on clinician-administered interviews. We therefore did not include studies that relied on self-report scales to make personality disorder diagnoses.⁴⁷⁻⁴⁹ We also did not

include studies in which the personality disorder diagnoses were based on unstructured clinical evaluations^{46,50-57} because these evaluations are less reliable^{58,59} and underdetect personality disorders.^{20,60} Studies in which diagnoses were based on chart review were also excluded^{61,62} because diagnoses were based on unstructured evaluations.

Reports based on overlapping samples were included only once. We included the data from Pica et al,⁶³ but not from Jackson et al⁶⁴ and Turley et al,⁶⁵ because the samples included the same patients. Similarly, the data in Colom et al⁶⁶ was not included because it overlaps with Vieta et al.^{67,68} Two papers from the Collaborative Longitudinal Personality Study reported the frequency of bipolar disorder in patients with BPD.^{69,70} The Skodol et al⁷⁰ report was based on all patients diagnosed with BPD, including BPD diagnosed in patients with other primary personality disorders. The McGlashan et al⁶⁹ report only examined the frequency of bipolar disorder in the 175 BPD patients with a principal diagnosis of BPD, and these patients were the most severe of the BPD group. We included the results from Skodol et al⁷⁰ because the sample was more representative of BPD patients in general, and the sample size was larger (240 vs 175). It was not clear if the two reports by Benazzi^{71,72} were overlapping. We concluded that they were based on different samples because the sample sizes were different, the second paper referenced the first without indicating that the samples overlapped, and the time frames over which the samples were collected were relatively brief (6 months and 10 months) and were consistent with the rate of recruitment over separate periods of time.

Coid et al⁷³ studied the frequency of bipolar disorder in prisoners with BPD who manifested affective instability.

Author	Bipolar diagnostic measure	Bipolar diagnostic criteria	Borderline diagnostic measure	Borderline diagnostic criteria	Psychiatric status at time of evaluation	Sample
Rossi ⁹²	SCID	DSM-III-R	SCID	DSM-III-R	Improved, not more than mildly depressed	Consecutive inpatients with depression, evaluated after significant improvement in depression
Ucok ⁹³	SCID	DSM-III-R	SCID	DSM-III-R	Euthymic	Euthymic outpatients
Vieta ⁶⁷	SCID	DSM-III-R	SCID	DSM-III-R	In remission	Bipolar I patients in primary care psychiatric setting
Vieta ⁶⁸	SADS-L	RDC	SCID	DSM-III-R	In remission	Bipolar II patients in primary care psychiatric setting
Wilson ⁸⁴	SCID	DSM-IV	SCID	DSM-IV	In depressive episode	¾ inpatients, ¼ outpatients
Zimmerman ⁷⁹	SCID	DSM-IV	SIDP	DSM-IV	Symptomatic	Consecutive outpatients at presentation

Table I. Continued

Because of the uncertain impact that requiring affective instability might have on the prevalence of bipolar disorder, this study was excluded. We also excluded the report by Schiavone et al⁷⁴ because the authors only recorded one personality disorder diagnosis even when patients had more than one. Thus, a patient with BPD who had another personality disorder that was considered more clinically significant than BPD would not be counted as having BPD. This would artificially reduce the number of patients with bipolar disorder who would be diagnosed with BPD.

The report by Zanarini and colleagues⁷⁵ on the frequency of Axis I disorders in patients with BPD was excluded because they indicated that patients with a history of a major psychotic disorder such as schizophrenia or bipolar disorder were excluded from the sample. It is therefore not surprising that no patients were diagnosed with bipolar disorder. We excluded studies of the fre-

quency of BPD in patients with cyclothymic temperament,⁷⁶ a construct that is not in *DSM-IV* and differs from cyclothymic disorder.

Frequency of borderline personality disorder in patients with bipolar disorder

Twenty-four studies reported the frequency of BPD in patients with bipolar disorder (*Tables I and II*). Most studies were of psychiatric outpatients, and only four were of samples of inpatients (or predominantly inpatients). The majority of the studies assessed BPD when the patients were in remission (n=9) or with no more than mild symptom severity (n=6); the remainder (n=9) assessed BPD when the patient was symptomatic. The Structured Clinical Interview for *DSM-IV* (or *DSM-III* or *DSM-III-R*) was the most commonly used measure to evaluate Axis I and Axis II disorders. Most reports

Author	Any bipolar disorder		Bipolar I disorder		Bipolar II disorder		Cyclothymia	
	Sample Size	% (n) with BPD	Sample Size	% (n) with BPD	Sample Size	% (n) with BPD	Sample Size	% (n) with BPD
Alnaes ⁸⁰			19	0.0 (0)			19	36.8 (7)
Barbato ⁸⁵			42	14.3 (6)				
Benazzi ⁷¹					50	12.0 (6)		
Benazzi ⁷²					78	11.5 (9)		
Brieger ⁸⁶			60	6.7 (4)				
Carpenter ⁸⁷			23	0.0 (0)				
Carpiniello ⁷⁸	57	31.6 (18)						
Comtois ⁸¹	34	23.5 (8)						
Dunayevich ⁸⁸			56	5.4 (3)				
Garno ⁷⁷	100	17.0 (17)						
Gasperini ⁸⁹	54	5.5 (3)						
George ⁹⁰			52	3.8 (2)				
Joyce ⁸²	26	11.5 (3)			19	31.6 (6)		
Loftus ⁹¹			51	19.6 (10)				
Perugi ⁸³					25	48.0 (12)		
Peselow ⁴⁰	47	23.4 (11)						
Pica ⁸³			26	11.5 (3)				
Preston ¹²³			35	40.0 (14)				
Ross ⁹²	71	29.6 (21)						
Ucok ⁹³			90	10.0 (9)				
Vieta ⁶⁷			129	6.2 (8)				
Vieta ⁶⁸					40	12.5 (5)		
Wilson ⁸⁴					30	50.0 (15)		
Zimmerman ⁷⁹	41	34.1 (14)	15	33.3 (5)	19	36.8 (7)		

Table II. Frequency of borderline personality disorder (BPD) in individuals with bipolar disorder.

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focused on either bipolar I or bipolar II disorder, and many did not discuss the bipolar I-bipolar II distinction. Two reports specified the number of patients with bipolar I and bipolar II disorder, but only reported the prevalence of BPD for the entire group without specifying the prevalence of BPD in the bipolar subtypes.^{77,78} Only two groups of investigators examined the frequency of BPD in patients with bipolar I and bipolar II disorder.^{67,79}

Across all studies, the frequency of BPD in the 1255 patients with bipolar disorder was 16.0% (n=201). In the 12 studies of 598 patients with bipolar I disorder, the prevalence of BPD was 10.7% (n=64). In the seven studies of 261 patients with bipolar II disorder, the prevalence of BPD was twice as high (22.9%, n=60). Only two groups of investigators reported data on both bipolar I and bipolar II disorder. In two separate reports Vieta et al^{67,68} found that BPD was diagnosed twice as frequently in patients with bipolar II disorder than bipolar I disorder (12.5% vs 6.2%). While they did not statistically compare these prevalence rates, we conducted a chi-square test based on the raw data provided in the two articles and found that the difference was not significant ($X^2 = 1.71$, ns). Similarly, Zimmerman et al⁷⁹ reported a higher prevalence of BPD in patients with bipolar II disorder, but the difference was not significant. Thus, while the summary across studies suggests a significantly higher rate of BPD in patients with bipolar II than bipolar I disorder, the only two studies that allowed for a direct comparison did not find a significant difference between the two groups. In the seven studies of 389 patients that either did not specify the type of bipolar disorder, or did not present results separately for bipolar I and bipolar II disorder, the rate of BPD was similar to the rate in patients with bipolar II disorder (20.8%, n=81).

Nine studies indicated that they assessed patients upon presentation for treatment or when the patients were symptomatic.^{71,72,77,79-84} Eight of these nine studies were of bipolar II disorder or unspecified bipolar disorder. Across these eight studies the prevalence of BPD was 22.5% (80/355), little different than the prevalence for the entire group of patients with bipolar II disorder or unspecified bipolar disorder. This suggests that state effects did not have a robust influence on the prevalence of BPD. Only one study directly examined the impact of psychiatric state on the prevalence of BPD. Peselow et al⁴⁰ interviewed patients upon presentation for treatment of hypomania, and again 8 weeks later after symptom

resolution, and found a small decrease in the prevalence of BPD (23.4% vs 17.0%). We are not aware of any comparable studies that interviewed bipolar patients while depressed and again after improvement in depressive symptoms.

Is borderline personality disorder the most frequent personality disorder in patients with bipolar disorder?

Fifteen studies examined the full-range of personality disorders in patients with bipolar disorder.^{40,63,67,68,80,82,85-93} In only four of the 15 studies BPD was the most frequent diagnosis.^{40,68,82,91} Histrionic personality disorder was the most common diagnosis in four studies^{63,67,85,89} and tied for the most common in another two studies,^{90,93} and obsessive-compulsive personality disorder was the most common in three studies^{86,87,92} and tied for the most common in another two studies.^{90,93} While this suggests that there is no clear evidence that BPD is the most common personality disorder in patients with bipolar disorder, it is noteworthy that BPD was the most frequent personality disorder diagnosis in the only two studies of bipolar II disorder.^{68,82}

Is borderline personality disorder more common in patients with bipolar disorder than psychiatric control groups?

Eight studies compared the frequency of BPD in patients with bipolar disorder and major depressive disorder.^{33,71, 81-83, 86,89,92} Four studies found no difference between the two groups,^{81,86,89,92} whereas three of the four studies of bipolar II disorder found a higher rate of BPD in the bipolar patients.^{33,71,82,83} Another study found no difference in the rate of BPD in patients with bipolar disorder and schizophrenia.⁶³ One study compared the frequency of Axis I disorders in a heterogeneous sample of psychiatric outpatients, and sufficient data was provided to calculate the rate of BPD in patients with different diagnoses.⁷⁹ BPD was significantly more frequent in patients with bipolar disorder than in patients with major depressive disorder, as well as more common than in patients with any psychiatric disorder. Another study of psychiatric outpatients with mixed diagnoses found a lower rate of BPD in patients with bipolar disorder.⁸⁰ Thus, four of ten studies found a significantly higher rate of BPD in patients with bipolar disorder compared with

a psychiatric control group, and three of these four positive studies were comparisons of bipolar II disorder versus major depressive disorder.

Frequency of bipolar disorder in patients with borderline personality disorder

Twelve studies reported the frequency of bipolar disorder in patients with BPD (*Tables III and IV*). Three studies of psychiatric outpatients of mixed diagnoses and one study of patients with a major depressive episode con-

tributed data to both this analysis as well as the previous analysis examining the frequency of BPD in patients with bipolar disorder.^{79-81,83} Most studies were of psychiatric outpatients, and only two were of samples of inpatients.^{94,95} In 10 of the 12 studies it was clear that the patients were symptomatic at the time of the evaluation, and in the remaining two studies symptom status was unstated.^{70,96} The Structured Clinical Interview for *DSM-IV* (or *DSM-III* or *DSM-III-R*) was the most commonly used measure to evaluate Axis I disorders, whereas there was more heterogeneity in the measures used to diag-

Author	Bipolar diagnostic measure	Bipolar diagnostic criteria	Borderline diagnostic measure	Borderline diagnostic criteria	Psychiatric status at time of evaluation	Sample
Akiskal ¹²⁷	Unspecified semistructured interview	<i>DSM-III</i>	Unspecified semistructured interview	<i>DSM-III</i>	Symptomatic	Consecutive outpatients
Alnaes ⁸⁰	SCID	<i>DSM-III</i>	SIDP	<i>DSM-III</i>	Symptomatic	Consecutive outpatients
Comtois ⁸¹	SCID	<i>DSM-III-R</i>	SCID	<i>DSM-III-R</i>	Upon presentation to outpatient program, symptomatic	Consecutive outpatients
Deltito ¹²⁸	SCID	<i>DSM-III-R</i>	SCID	Unstated	Unstated	Patients in current treatment, diagnosed clinically with BPD which was confirmed with SCID
Hudziak ¹²⁹	<i>DSM-III-R</i> checklist	<i>DSM-III-R</i>	DIBR	DIBR	Unstated but symptomatic	In and outpatients clinically diagnosed with BPD
Links ⁹⁴	SADS	RDC	DIB	DIB	Symptomatic	Inpatients without a primary diagnosis of substance use disorder
Perugi ⁸³	SCID	<i>DSM-III-R</i>	SCID	<i>DSM-III-R</i>	Symptomatic	Outpatients (71%) and day hospital patients (29%) with atypical depression
Pope ⁶¹	Chart	<i>DSM-III</i>	DIB	<i>DSM-III</i>	Symptomatic	Consecutive psychiatric inpatients administered the DIB who scored 6 and above
Prasad ⁹⁶	DIS	<i>DSM-III</i>	DIB	<i>DSM-III</i>	Unstated	Outpatients with clinically diagnosed BPD who did not have major affective disorder, schizophrenia, or organic brain syndrome
Skodol ⁷⁰	SCID	<i>DSM-IV</i>	DIPD	<i>DSM-IV</i>	Unstated	Referred for study of personality disorders
Zanarini ⁹⁵	SCID	<i>DSM-III-R</i>	DID, DIBR	<i>DSM-III-R</i> & DIBR	Psychiatric inpatients	Psychiatric inpatients with clinical diagnosis of probable PD. BPD was severe because 2 criteria sets met. Patients with bipolar I disorder excluded
Zimmerman ⁷⁹	SCID	<i>DSM-IV</i>	SIDP-IV	<i>DSM-IV</i>	symptomatic	Consecutive outpatients at presentation

Table III. Methods of studies of the frequency of bipolar disorder in individuals with borderline personality disorder (BPD). *DSM*, *Diagnostic and Statistical Manual for Mental Disorders*; DIB, Diagnostic Interview for Borderlines; DIBR, Diagnostic Interview for Borderlines Revised; DIPD, Diagnostic Interview for Personality Disorders; SCID, Structured Clinical Interview for *DSM-IV* (or *DSM-III-R*); DIS, Diagnostic Interview Schedule; SIDP, Structured Interview for DSM Personality; SADS-L, Schedule for Affective Disorders and Schizophrenia Lifetime version; RDC, Research Diagnostic Criteria

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nose BPD. Half of the studies examined the frequency of both bipolar I and bipolar II disorder. Two studies reported both current and lifetime rates of bipolar disorder, and we included the data on lifetime rates.^{79,94}

A difficulty in summarizing the data is that studies varied in the breadth of their diagnosis of bipolar disorder. Only one study reported rates of bipolar I, bipolar II, and cyclothymic disorder.⁹⁴ Across all 12 studies, the frequency of any bipolar disorder in the 1151 patients was 14.1% (n=162). The largest study, by Zanarini et al,⁹⁵ excluded patients with bipolar I disorder, and the rate of any bipolar disorder in this study was amongst lowest of the studies summarized in *Table IV*. When the results of this study are excluded, then the rate of any bipolar disorder across the remaining 11 studies was 16.3% (126/772). Six studies reported rates of both bipolar I and bipolar II disorder. Across these six studies the rate of either bipolar I or bipolar II disorder was 19.1% (90/470).

In the nine studies of 634 patients that assessed bipolar I disorder, the prevalence was 9.3% (n=59). In the eight studies assessing bipolar II disorder, the prevalence was 10.1% (n=101). Limiting the analysis to the six studies that reported the rates of both bipolar I and bipolar II disorder, the results were the same (bipolar I disorder, 8.9%; bipolar II disorder, 10.2%). Only three studies reported the rate of cyclothymic disorder, and across these three studies the overall prevalence was 12.9% (30/232).

Co-occurrence of bipolar disorder and borderline personality disorder in nonpatient samples

To this point we have summarized studies of psychiatric patients. Only four studies of nonpatient samples have examined the association between bipolar disorder and BPD. Because comorbidity may be associated with seeking treatment, an examination of the degree of co-occurrence should examine non-treatment-seeking samples. While there are many studies of the epidemiology of personality disorders,⁹⁷ we are aware of only four studies that reported bipolar-BPD comorbidity.

Zimmerman and Coryell⁹⁸ assessed *DSM-III* Axis I and Axis II disorders in 797 first-degree relatives of healthy controls and psychiatric patients. Trained interviewers experienced in evaluating psychiatric patients administered the fully structured Diagnostic Interview Schedule (DIS)⁹⁹ for Axis I disorders and the semi-structured SIDP for Axis II disorders. BPD was the third most frequently diagnosed personality disorder in individuals with bipolar disorder (obsessive-compulsive and antisocial personality disorders were the most frequent diagnoses). The rate of BPD was nearly twice as high in bipolar disorder than major depressive disorder (12.5% vs 6.9%), though this difference was not significant. The rate of bipolar disorder in the subjects with BPD was 15.4%, significantly higher than the rate in individuals

Author	n of BPD sample	% (n) with Any bipolar disorder	% (n) with Bipolar I disorder	% (n) with Bipolar II disorder	% (n) with Cyclothymia
Akiskal ¹²⁷	100		Excluded	17.0 (17) ^b	7.0 (7)
Alnaes ⁸⁰	44		0.0 (0)		15.9 (7)
Comtois ⁸¹	38	21.1 (8)			
Deltito ¹²⁸	16	31.25 (5)	12.5 (2)	18.7 (3)	
Hudziak ¹²⁹	87		16.1 (14)		
Links ^{94 a}	88		5.9 (6)	9.6 (8)	17.9 (16)
Perugi ⁸³	46		2.2 (1)	26.1 (12)	
Pope ⁶¹	33		9.1 (3)		
Prasad ⁹⁶	21	23.8 (5)	16.7 (4)	4.8 (1)	
Skodo ¹⁷⁰	240		9.2 (22)	6.9 (17)	
Zanarini ⁹⁵	379		Excluded	9.5 (36)	
Zimmerman ⁷⁹	59		8.5 (7)	11.9 (7)	

Table IV. Frequency of bipolar disorder individuals with borderline personality disorder (BPD). a, Links et al present lifetime and current rates of bipolar disorder; we included lifetime rates. The authors presented data for mania, hypomania, bipolar manic, and bipolar hypomanic. It was unclear what distinctions were being made. We included the rates for lifetime mania and hypomania which were higher than the respective bipolar rates. b, Bipolar II disorder required only a 2-day duration of hypomanic symptoms, and could include pharmacologically induced hypomanic episodes.

with no personality disorder (15.4% vs 0.9%), but not significantly different than the rate in individuals with any other personality disorder (7.0%).

Swartz et al¹⁰⁰ constructed an algorithm to approximate the diagnosis of BPD from the DIS and examined the prevalence of BPD and its relationship to Axis I disorders in the 1541 general population participants at the Duke University site of the Epidemiologic Catchment Area study. The rate of *DSM-III* bipolar disorder was significantly higher in subjects with BPD than without (14.1% vs 0.5%), results that were very similar to the findings of Zimmerman and Coryell.⁹⁸

Lenzenweger et al¹⁰¹ directly interviewed 214 respondents in the National Comorbidity Survey Replication¹⁰² with the International Personality Disorder Examination (IPDE).¹⁰³ These subjects also completed the IPDE screening questionnaire. A multiple imputation method was used to approximate the diagnosis of BPD in the NCS-R respondents who completed the IPDE screening questionnaire but were not administered the diagnostic interview. *DSM-IV* Axis I diagnoses were based on the fully structured Composite International Diagnostic Interview.¹⁰⁴ The Axis I diagnostic information presented in the article focused on diagnoses in the past year, and the data for bipolar disorder combined bipolar I and bipolar II disorder. The rate of bipolar I or II disorder in subjects with BPD (14.8%) was nearly identical to the rate reported by Zimmerman and Coryell⁹⁸ and Swartz et al¹⁰⁰. The prevalence of BPD in subjects with bipolar I or bipolar II disorder was 15.5%. Odds ratios (OR) were computed controlling for demographic variables. The odds ratio between BPD and bipolar disorder (12.5) was higher than all other odds ratios between BPD and Axis I disorders except any impulse control disorder (OR=14.4) and intermittent explosive disorder (OR=12.5).

Grant et al¹⁰⁵ conducted face-to-face interviews with approximately 35 000 participants in the second wave of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Diagnoses were based on the *DSM-IV* version of the fully structured Alcohol Use Disorder and Associated Disabilities Interview Schedule.¹⁰⁶ The overall rate of BPD was 5.9%, higher than the rates reported in other epidemiological surveys.^{101,107,108} The prevalence of BPD in respondents with a lifetime history of bipolar disorder was high (bipolar I, 35.9%; bipolar II, 26.7%). The rates were even higher when the analyses were limited to bipolar diagnoses in

the past 12 months (bipolar I, 50.1%; bipolar II, 39.4%). The higher rates for diagnoses based on the past year are likely due to BPD being associated with greater chronicity and recurrence of bipolar disorder episodes. The lifetime prevalence of bipolar I and bipolar II disorder among individuals with BPD was 31.8% and 7.7%, respectively. Grant et al¹⁰⁵ computed odds ratios between BPD and the lifetime rate of 15 Axis I disorders controlling for demographic variables and found that the odds ratio was highest for bipolar I disorder (OR=9.9), whereas for bipolar II disorder several disorders had higher odds ratios. When the presence of other Axis I disorders was also controlled, then lifetime diagnoses of bipolar I and bipolar II disorder had the highest odds ratios with BPD. However, another report from the Wave 2 assessment in the NESARC study, on the association between narcissistic personality disorder and Axis I disorders raise questions about the specificity of the association between BPD and bipolar disorder. Stinson et al¹⁰⁹ computed odds ratios between narcissistic personality disorder and the lifetime rate of the same 15 Axis I disorders controlling for demographic variables and, similar to the results of Grant et al¹⁰⁵ on BPD, found that the odds ratio was highest for bipolar I disorder (OR=5.2), whereas for bipolar II disorder several disorders had higher odds ratios.

To summarize the results of these four epidemiological and quasi-epidemiological studies, three studies were consistent in finding that approximately 15% of the community respondents with BPD were diagnosed with bipolar disorder,^{98,100,101} whereas the NESARC data was an outlier with a combined bipolar I and bipolar II prevalence of nearly 40%.¹⁰⁵ The NESARC study was also an outlier in finding a higher prevalence of bipolar disorder than other epidemiologic studies. It is not surprising that significant odds ratios were found between bipolar disorder and BPD. However, BPD was significantly associated with other Axis I disorders as well. The specificity of the relationship between BPD and bipolar disorder was not clearly established. The only report of the full range of personality disorders found that BPD was the third most frequent diagnosis in adults with bipolar disorder, and that the rate of bipolar disorder in subjects with BPD was not significantly higher than the rate in subjects with other personality disorders.⁹⁸ However, the sample size in the study was relatively small, and diagnoses were based on *DSM-III* which had not yet officially recognized bipolar II disorder.

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Summary and conclusions

The goal of this review was to examine the relationship between bipolar disorder and BPD, particularly the specificity of the relationship. While many studies have examined comorbidity rates, particularly in psychiatric patients, methodological considerations limit some of the conclusions that can be drawn.

How frequent is BPD in bipolar patients? And does this vary by subtype of bipolar disorder?

Across studies approximately 10% of patients with BPD had bipolar I disorder and another 10% had bipolar II disorder. Thus, a total of about 20% of patients with BPD were diagnosed with bipolar disorder. Likewise, approximately 20% of bipolar II patients were diagnosed with BPD, though only 10% of bipolar I patients were diagnosed with BPD. Psychiatric status at time of assessment did not appear to have an influence on these rates.

Most of the studies in the present review were based on small sample sizes; only 1 of the 24 studies summarized in *Table II* had a sample size greater than 100. Small sample sizes result in large confidence intervals, and this contributes to the wide variation in prevalence rates. The small-scale studies typically focused on only one bipolar disorder subtype, with only two investigators providing information on both bipolar I and bipolar II disorder.

Much has been written about the bipolar-borderline link, and some authors have suggested that BPD is on the bipolar spectrum.^{76,110} It was therefore surprising that in the 15 studies examining the full range of personality disorders in patients with bipolar disorder that BPD was the most frequent in only four studies. Obsessive-compulsive and histrionic personality disorders were more frequently the most commonly diagnosed personality disorders. This raises questions about the specificity of the bipolar-borderline link. However, BPD was the most frequent personality disorder in the only two studies of bipolar II disorder. Consistent with the stronger association between BPD and bipolar II disorder than bipolar I disorder, three of the four studies comparing the prevalence of BPD in bipolar II patients with psychiatric control groups were significant versus one of the six studies of bipolar I or unspecified bipolar disorder.

Why is there a seemingly stronger link between bipolar II disorder and BPD? We believe that this is primarily related to diagnostic error. As one of us discussed elsewhere, when diagnosis is based on the presence of symp-

tom episodes that occurred in the past, as is the case with bipolar disorder in currently depressed patients, diagnostic clarity is sometimes elusive thereby resulting in some false-negative as well as false-positive diagnoses.¹¹¹ *DSM-IV* is a categorical system that provides descriptive diagnostic criteria of psychiatric syndromes. The definition of mental disorder in *DSM-IV* notes that these syndrome descriptions represent underlying behavioral, psychological, or biological dysfunction, albeit imperfect representations of the potentially unknown, underlying core dysfunction. The descriptive diagnostic criteria should not be considered the last word on whether a patient has the illness in question, but instead the criteria should be conceptualized as a type of test for the underlying, etiologically-defined, illness. Accordingly, as with any other diagnostic test, diagnoses based on the *DSM-IV* criteria produce some false positive and some false negative results. That is, some patients who meet the *DSM-IV* diagnostic criteria will not have the illness (ie, false positives), and some who do not meet the criteria because their symptoms fall below the *DSM-IV* diagnostic threshold, will have the illness and incorrectly not receive the diagnosis (ie, false negatives). According to this conceptualization, the gold standard with which *DSM-IV* diagnoses are being compared is a not-yet-discovered index of illness such as a biomarker.

The lack of congruence between phenomenological diagnosis and underlying pathophysiology is one cause of diagnostic error. A second cause is related to the limits of the accuracy of retrospective recall and reporting. Transient episodes of affective instability and emotional lability associated with borderline personality disorder might be confused with hypomanic episodes, thereby resulting in false-positive diagnoses.^{33,112} This is not to suggest that affective instability is pathognomonic for borderline personality disorder, but rather to illustrate how phenomenological similarities might result in diagnostic error. This error is likely greater with bipolar II disorder than bipolar I disorder, and we would hypothesize would be even greater if the diagnostic thresholds for bipolar disorder are lowered below the current *DSM-IV* standard. Thus, some patients diagnosed with both borderline and bipolar II disorders are likely to have false-positive bipolar disorder diagnoses. And some likely have false positive BPD diagnoses. In clinical practice additional sources of diagnostic error include clinical unfamiliarity with Axis II disorders,¹¹³ the perception that bipolar disorder is more easily treated (thus “erring on

the side of caution”),¹¹⁴ the desire to protect patients from a stigmatizing diagnosis,¹¹⁵ or lower reimbursement rates for treating Axis I vs Axis II disorders.¹¹⁵ To us, the question is not whether diagnostic error exists, but rather which type of error predominates and what can be done to reduce such errors.

There is much need for research comparing patients with BPD to bipolar disorder, particularly bipolar II disorder. As noted in the introduction, few studies have compared these groups. Moreover, the few studies that have directly compared the two disorders have been based on small samples and examined a limited number of variables.^{84,116-120} We are not aware of any study that has focused on depressed patients presenting for treatment and compared those who are diagnosed with either bipolar II disorder or BPD—a clinically important distinction faced by clinicians. A direct comparison of these two groups of patients could identify variables that would assist clinicians in making this differential diagnosis, and subsequently in making treatment decisions. Similarly, few direct comparisons of patients with bipolar disorder and BPD have been conducted with respect to treatment. Even fewer include groups of patients with comorbid bipolar disorder and BPD in their comparisons, and those that do neglect one of the other two groups. Similar to other studies reviewed here, existing treatment studies suffer from small sample sizes,^{56,121} use unclear diagnostic methods,¹²² or rely on atypical measures to diagnose one or both disorders.¹²³ With some exceptions, they also largely use pharmacotherapy, typically with medications such as mood stabilizers that have been shown to be effective for treatment of bipolar disorder. Importantly, preferential use of medication trials neglects the psychosocial and behavior change interventions inherent in treatments for BPD. More research is needed on to what degree these disorders benefit from various treatments relative to one another, and also on best treatment practices for comorbid BPD and bipolar disorder.

An examination of comorbidity, and the specificity of the association, is informative regarding the link between BPD and the bipolar spectrum; however, the most informative approach towards answering this question is to compare depressed patients with and without BPD on validators that are specific for bipolar disorder.¹²⁴ Thus, the demonstration that compared with depressed patients without BPD, depressed patients with BPD have more anxiety disorders, more substance-use disorders, and a younger age of onset, does not support the bipolar spectrum hypothesis because these differences would be expected for BPD as well. Instead, studies attempting to demonstrate that BPD is part of the bipolar spectrum should focus on variables that are specific to bipolar disorder such as a family history of bipolar disorder which would not be expected to be elevated in BPD probands unless BPD was part of the bipolar spectrum.

In the final analysis though we believe that the results of the present review challenge the notion that BPD is part of the bipolar spectrum. While the comorbidity rates are substantial, each disorder is nonetheless diagnosed in the absence of the other in the vast majority of cases (80% to 90%). In studies examining personality disorders broadly, other PDs such as histrionic and obsessive-compulsive were more commonly diagnosed in bipolar patients than was BPD. Although not reviewed here, the converse is also true: other axis I disorders such as major depression, substance abuse, and post-traumatic stress disorder are also more commonly diagnosed in patients with BPD than is bipolar disorder.¹¹⁵ In both of these cases, rates of comorbidity alone have not led to the argument that the disorders exist along the same spectrum. In valid cases of co-occurrence, it is possible that this reflects a common etiology where risk factors for one disorder lead to the co-occurrence of the other.^{125,126} □

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La relación entre trastorno de personalidad borderline y trastorno bipolar

En los pacientes que buscan un tratamiento para la depresión es importante, clínicamente, reconocer tanto el trastorno bipolar como el trastorno de personalidad borderline (TPB) y es primordial poder distinguirlos. Las investigaciones que consideran que el TPB debe ser incluido como parte del espectro bipolar llegan a distintas conclusiones. Se revisó la pregunta más estudiada acerca de la relación entre el TPB y el trastorno bipolar: ¿cuál es su concordancia diagnóstica? Entre los estudios se encontró que aproximadamente el 10% de los pacientes con TPB tenía un trastorno bipolar I y otro 10% tenía un trastorno bipolar II. Asimismo, aproximadamente el 20% de los pacientes bipolares II fue diagnosticado con TPB, en cambio sólo el 10% de los bipolares I tuvo ese diagnóstico. A pesar de que las cifras de comorbilidad son considerables, cada trastorno es diagnosticado en ausencia del otro en la gran mayoría de los casos (80% a 90%). En los estudios que examinan en general los trastornos de personalidad, los pacientes bipolares fueron diagnosticados más comúnmente con otros trastornos de la personalidad que con el TPB. Asimismo, lo inverso también es verdadero: otros trastornos del eje I como la depresión mayor, el abuso de sustancias y el trastorno por estrés postraumático también fueron diagnosticados con mayor frecuencia en pacientes con TPB que en el trastorno bipolar. Estos hallazgos ponen en tela de juicio la idea que el TPB es parte del espectro bipolar.

Relation entre le trouble de personnalité « borderline » et la maladie bipolaire

Il est important de reconnaître cliniquement le trouble bipolaire et la personnalité « borderline » (PBL) chez les patients demandant un traitement antidépresseur, et de les distinguer l'un de l'autre. Pour la recherche, l'appartenance de la PBL au cadre des troubles bipolaires a donné lieu à des conclusions divergentes. Nous analysons la question la plus étudiée sur la relation entre la PBL et le trouble bipolaire : leur concordance diagnostique. Dans les études, environ 10 % des patients ayant une PBL sont atteints de trouble bipolaire I et 10 % de trouble bipolaire II. De même, environ 20 % des patients bipolaires II souffrent de PBL alors que seulement 10 % des patients bipolaires I ont une PBL. Les taux de comorbidité sont importants mais chaque maladie est néanmoins diagnostiquée en l'absence de l'autre dans la grande majorité des cas (80 à 90 %). Dans les études s'intéressant aux troubles de la personnalité de manière plus large, les autres troubles de la personnalité ont été plus fréquemment diagnostiqués chez les patients bipolaires. L'inverse est également vrai : les autres troubles de l'axe I comme la dépression majeure, les abus de substance et les états de stress post-traumatique sont plus fréquemment rencontrés chez les patients PBL que chez les patients bipolaires. Ces résultats remettent en question la notion de l'appartenance de la PBL au cadre bipolaire.

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