

Bipolar disorder or something else?

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Ms. S, age 31, is found intoxicated with empty pill bottles in her purse. She was diagnosed with bipolar disorder at age 12, but has no history of elevated mood. Was she misdiagnosed?



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CASE Unclear diagnosis

Police find Ms. S, age 31, extremely intoxicated and drinking alcohol in her car in a city park parking lot. In the emergency room, she becomes increasingly somnolent and clinicians intubate her trachea to protect her airway. Lab testing shows she has elevated acetaminophen and lithium serum levels, and she is transferred to our hospital for further management after being started on N-acetylcysteine to treat acetaminophen toxicity. Her “ex-fiancé,” the father of her 2 children, saw her earlier the day of the episode and says she was distraught, intoxicated, and had several empty pill bottles in her purse.

In our hospital, Ms. S’ lithium level increases from 2.3 mEq/L to a peak of 5.32 mEq/L, and she undergoes hemodialysis. On hospital day 2, her serum lithium level is trending downward. After Ms. S is able to breathe spontaneously, her trachea is extubated and her hemodialysis line is removed. A psychiatric consultation is obtained, but she is unable to provide a coherent history and the treating clinicians believe she has delirium caused by multiple factors.

On hospital day 3, Ms. S’ delirium clears enough for her to engage in an interview, and she is transferred to our inpatient psychiatry ward for further monitoring and stabilization.

She reports that she was diagnosed with bipolar disorder (BD) at age 12, when she

faced multiple psychosocial stressors, including physical abuse by her mother’s boyfriend. She took several psychotropics—although she cannot remember which ones—until age 14, when she stopped all medications until the year before her current hospitalization. Although throughout adolescence and adulthood Ms. S experienced chronic irritability, anxiety, impulsive behavior, poor self-esteem, abusive relationships, self-cutting, and depressed mood, she maintains that she felt worse when she was taking psychotropics and doubts the BD diagnosis. She attributes her longstanding mood issues to low self-worth, a “codependent nature,” and a tendency to gravitate toward abusive relationships. Although she admits to experimenting with several illicit drugs during adolescence, she denies more recent substance use and states she drinks alcohol only once every few months.

What is the most likely diagnosis that led to her overdose?

- a) substance-induced mood disorder
- b) borderline personality disorder (BPD)
- c) inadequately treated BD
- d) major depressive disorder (MDD)

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continued

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Patients incorrectly diagnosed with BD may be likely to have a personality disorder, particularly BPD

The authors' observations

BD is underdiagnosed in several patient populations, such as individuals previously diagnosed with MDD.¹⁻³ Misdiagnosis can have severe implications, including delay in receiving treatment with effective medications (eg, mood stabilizers) or use of agents that can induce mania or rapid-cycling, such as antidepressants. Perhaps in response to this concern, in recent years clinicians increasingly have diagnosed BD in adolescents and adults. An analysis of a national database of physician practices found a 40-fold increase in office visits for BD among youth and a near doubling among adults from 1994 to 2003.⁴

Although underdiagnosis of BD remains important, some researchers have suggested that overdiagnosis may be more prevalent and equally harmful. In a study of 180 patients being treated for depression in a family care clinic, there was a 21.6% initial underdiagnosis rate among those eventually found to have BD.¹ However, among 43 patients with a prior BD diagnosis, the diagnosis was not confirmed in 33%.¹ In a study of 700 psychiatric outpatients in Rhode Island, only 43% of 145 patients who reported a prior BD diagnosis had that diagnosis confirmed.⁵ Three times as many patients were overdiagnosed with BD as underdiagnosed.

Are there characteristics common to individuals incorrectly diagnosed with BD? In a study that compared patients who had been mistakenly diagnosed with BD with those who had not been diagnosed with BD, the overdiagnosis group was significantly more likely to be diagnosed with a personality disorder, in particular borderline or antisocial personality disorder.⁶ Only lifetime and current BPD, current posttraumatic stress disorder (PTSD), and lifetime impulse control disorders were independently associated with BD overdiagnosis. The odds ratio for overdiagnosis of BD in patients found to have BPD was 3.7.

Which of the following would be the least appropriate feature of Ms. S' treatment plan?

- a) refer her for alcohol abuse treatment
- b) restart lithium and titrate the dosage until her symptoms resolve
- c) speak to her friends and family to help construct an adequate suicide safety plan
- d) refer her to dialectical behavior therapy (DBT)
- e) consider short-term pharmacologic intervention to stabilize affective dysregulation

EVALUATION Rethink the diagnosis

In the last few months, Ms. S had complained to her primary care provider (PCP) of worsening anxiety and depressed mood. She was the victim of ongoing physical and emotional abuse by her ex-fiancé and was concerned that she may lose custody of her 2 sons. Approximately 8 months before admission, Ms. S' PCP prescribed lithium, 450 mg, 3 times a day, for "mood stabilization" and depression because she'd already been diagnosed with BD. This was the first mood stabilizer she'd taken since she was 14. She also was taking unknown doses of hydrocodone/acetaminophen, cyclobenzaprine, and tramadol for pain and temazepam for insomnia. Ms. S continued to suffer from labile and depressed mood, and fought with her ex-fiancé and legal authorities to maintain custody of her 2 children until she was found in the park.

Throughout her hospitalization she denies that she attempted suicide that day, and maintains that this incident was caused by unintentional mismanagement of her medications. Although she continues to have a sense of low self-worth, she denies feeling depressed; in contrast, she says she feels like she has a "new lease on life." During several interviews she cannot provide a history of any prolonged (ie, several days) episodes of elevated mood, increased goal-directed behavior, decreased need for sleep, tangential thought, pressured speech, or other symptoms that suggest hypomania or mania. She does not endorse prolonged peri-



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Table 1

DSM-IV-TR diagnostic criteria for borderline personality disorder

A pervasive pattern of instability of interpersonal relationships, self-image, and affects, and marked impulsivity, as indicated by ≥ 5 of the following:
1) Frantic efforts to avoid real or imagined abandonment
2) A pattern of unstable and intense interpersonal relationships characterized by alternating between extremes of idealization and devaluation
3) Identity disturbance: markedly and persistently unstable self-image or sense of self
4) Impulsivity in ≥ 2 areas that are potentially self-damaging (eg, spending, sex, substance abuse, reckless driving, binge eating)
5) Recurrent suicidal behavior, gestures, or threats, or self-mutilating behavior
6) Affective instability due to marked reactivity of mood (eg, intense episodic dysphoria, irritability, or anxiety usually lasting a few hours and rarely more than a few days)
7) Chronic feelings of emptiness
8) Inappropriate, intense anger or difficulty controlling anger (eg, frequent displays of temper, constant anger, recurrent physical fights)
9) Transient, stress-related paranoid ideation or severe dissociative symptoms
Source: Reference 7

ods of neurovegetative symptoms that would indicate a major depressive episode.

We feel that Ms. S' symptoms of affective dysregulation, impulsivity, and interpersonal dysfunction are consistent with BPD, and we determine that she meets 6 of the 9 DSM-IV-TR diagnostic features of BPD (≥ 5 are required for a BPD diagnosis) (**Table 1**).⁷ Ms. S describes efforts to avoid abandonment, unstable and intense interpersonal relationships, marked and persistent unstable self-image, recurrent suicidal and self-mutilating behavior, affective instability, and chronic feelings of emptiness. She is discharged to follow up with a psychotherapist and family practitioner. She is not continued on any psychotropic medications.

The authors' observations

Although it can be difficult to accurately diagnose psychiatric illness during a brief inpatient hospitalization, several clinicians who cared for Ms. S felt that her presentation was more consistent with BPD than BD. Her case is an example of the potential harm of incorrectly diagnosing personality-disordered patients with BD. Ms. S is impulsive and used lithium—a medication that is the standard of care for BD—in an

overdose, which lead to a costly and dangerous hospitalization marked by a difficult tracheal intubation and hemodialysis.

Distinguishing BD and BPD

There is considerable overlap in symptoms of BD and BPD. Although the episodic nature of BD is well differentiated from the more chronic course of BPD, many hypomania and mania symptoms are similar to those of BPD (**Table 2, page 46**).⁷ For example, patients with BD or BPD may exhibit impulsive behavior and labile moods. Substance use, risky and self-destructive behaviors, and inflammatory interpersonal relationships can occur in both disorders. Some researchers have suggested that pathophysiologically, BPD may fall on a spectrum of bipolar illness, and have proposed a clinical entity they call bipolar type IV or ultra-rapid cycling BD.^{2,8,9} There may be more co-occurrence of BD with BPD than would be expected by chance¹⁰; 1 review of BPD studies found the rate of comorbid BD ranged from 5.6% to 19%.¹¹ However, because of differences in several factors—including phenomenology, family prevalence, longitudinal course, and medication

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Unlike BPD, BD is episodic; however, many hypomania and mania symptoms are similar to those of BPD

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Clinicians may be more likely to diagnose a condition that responds to medication (ie, BD) than one that does not (ie, BPD)

Table 2

DSM-IV-TR diagnostic criteria for a manic episode

A) A distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting ≥ 1 week (or any duration if hospitalization is necessary)
B) During the period of mood disturbance, ≥ 3 of the following symptoms have persisted (4 if the mood is only irritable) and have been present to a significant degree: <ol style="list-style-type: none"> 1) Inflated self-esteem or grandiosity 2) Decreased need for sleep (eg, feels rested after only 3 hours of sleep) 3) More talkative than usual, or pressure to keep talking 4) Flight of ideas, or subjective experience that thoughts are racing 5) Distractibility (ie, attention too easily drawn to unimportant or irrelevant external stimuli) 6) Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation 7) Excessive involvement in pleasurable activities that have a high potential for painful consequences (eg, engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)
C) The symptoms do not meet criteria for a mixed episode
D) The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features
E) The symptoms are not due to the direct physiological effects of a substance (eg, a drug of abuse, a medication, or other treatment) or a general medical condition (eg, hyperthyroidism)
The DSM-IV-TR diagnostic criteria for a hypomanic episode are similar to criteria for a manic episode, except: <ul style="list-style-type: none"> - For criterion A the episode must last ≥ 4 days rather than 1 week - The disturbance in mood and change in functioning are observable by others, but the episode is not severe enough to cause marked impairment in social or occupational functioning, or to necessitate hospitalization, and there are no psychotic features

Source: Reference 7

response—some researchers have concluded that evidence does not support categorizing BPD as part of a bipolar spectrum.¹⁰⁻¹⁴ Nonetheless, BPD and other personality disorders often co-occur with axis I disorders, including MDD, BD, or PTSD.

Some research has suggested that the increasing availability and marketing campaigns of medications to treat BD may promote diagnosis of the disorder.¹⁵ Zimmerman¹⁵ hypothesizes that physicians may be more likely to diagnose a condition that responds to medication (ie, BD) than one that is less responsive (ie, BPD). Financial compensation for treating axis I disorders is significantly better than for treating personality disorders.¹⁶ The inpatient setting confers barriers to accurately diagnosing personality disorders,

including limits on the amount of time that clinicians can spend with patients or ability to communicate with sources of collateral information. A patient's observed personality and behaviors while hospitalized may not accurately reflect his or her personality and behaviors in that patient's "natural" environment.

Several diagnostic strategies can help distinguish BPD from BD. For BD to be the primary diagnosis, a patient must have had a hypomanic or manic episode. Sustained episodes of elation or extreme irritability without evident stressors suggest BD rather than BPD.¹⁰ According to Gunderson et al,¹⁰ "repeated angry outbursts, suicide attempts, or acts of deliberate self harm that are reactive to interpersonal stress and reflect extreme rejection sensitiv-

ity are axiomatic of borderline personality disorder.” In a review of clinical practice, Gunderson¹⁷ found that hypersensitivity to rejection and fearful preoccupation with expected abandonment are the most distinctive characteristics of BPD patients. He suggested that clinicians can establish the diagnosis by asking patients directly if they believe the criteria for BPD characterize them, which also can help a patient to accept the diagnosis.

Finally, during a short hospitalization, it can be helpful to obtain collateral information from the patient’s friends and family or further characterize the time course of symptoms and diagnostic features in the patient’s natural environment. Clinicians who are reluctant to diagnose BPD in an inpatient setting could suggest the presence of borderline traits or discuss the possibility of the BPD diagnosis in docu-

mentation (eg, in the assessment or formulation). Doing so would avoid a premature BPD diagnosis and allow outpatient providers to confirm or rule out personality disorder diagnoses over time. It is important to screen patients with BPD for co-occurring axis I disorders, including BD, MDD, PTSD, and substance abuse.

A false-positive BD diagnosis in patients with BPD has serious treatment implications. Antipsychotics, antidepressants, and anticonvulsants have been used to target BPD symptoms such as affective dysregulation, impulsivity, and cognitive/perceptual abnormalities, but no medications are FDA-approved for treating BPD. American Psychiatric Association guidelines recommend symptom-based pharmacologic strategies for BPD,¹⁸ although some researchers believe that these recommendations are out-of-date and not

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Hypersensitivity to rejection and fearful preoccupation with expected abandonment are distinctive characteristics of BPD

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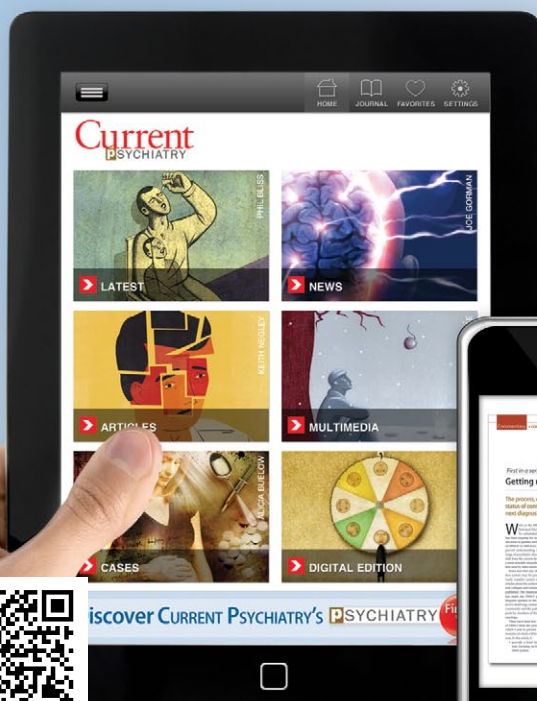


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Some evidence suggests pharmacotherapy can have modest short-term benefits on specific BPD symptoms

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- National Education Alliance Borderline Personality Disorder. www.borderlinepersonalitydisorder.com.
- Hoffman PD, Steiner-Grossman P. *Borderline personality disorder: meeting the challenges to successful treatment*. Philadelphia, PA: Haworth Press; 2008.

Drug Brand Names

Cyclobenzaprine • Flexeril	Temazepam • Restoril
Hydrocodone/acetaminophen	Tramadol • Ultram
• Lorcet, Vicodin, others	
Lithium • Eskalith, Lithobid	

Disclosure

The authors report no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

evidence-based.^{17,19} Some evidence suggests pharmacotherapy can have modest short-term benefits on specific BPD symptoms, but no data suggest that medication can reduce the severity of BPD or lead to remission.¹⁹⁻²³ Just 1 randomized controlled trial (N = 17) has examined lithium for BPD and found no effect on mood.^{11,24}

Misdiagnosis of BD in the context of BPD may create unrealistic expectations regarding the potential efficacy of medications for relieving symptoms. Patients may be diverted from potentially helpful psychotherapeutic treatments—such as DBT or mentalization therapy—which evidence suggests can effectively reduce symptoms, the need for additional treatments, and self-harm or suicidal behaviors.^{10,17,19} Evidence from long-term longitudinal studies suggests that psychosocial or psychotherapeu-

tic treatment may protect against suicide in BPD patients.²⁵

References

1. Hirschfeld RM, Cass AR, Holt DC, et al. Screening for bipolar disorder in patients treated for depression in a family medicine clinic. *J Am Board Fam Pract*. 2005;18(4):233-239.
2. Ghaemi SN, Ko JY, Goodwin FK. "Cade's disease" and beyond: Misdiagnosis, antidepressant use, and a proposed definition for bipolar spectrum disorder. *Can J Psychiatry*. 2002;47(2):125-134.
3. Bowden CL. Strategies to reduce misdiagnosis of bipolar depression. *Psychiatr Serv*. 2001;52(1):51-55.
4. Moreno C, Laje G, Blanco C, et al. National trends in the outpatient diagnosis and treatment of bipolar disorder in youth. *Arch Gen Psychiatry*. 2007;64(9):1032-1039.
5. Zimmerman M, Ruggiero CJ, Chelminski I, et al. Is bipolar disorder overdiagnosed? *J Clin Psychiatry*. 2008;69(6):935-940.
6. Zimmerman M, Ruggiero CJ, Chelminski I, et al. Psychiatric diagnoses in patients previously overdiagnosed with bipolar disorder. *J Clin Psychiatry*. 2010;71(1):26-31.
7. *Diagnostic and statistical manual of mental disorders*, 4th ed, text rev. Washington, DC: American Psychiatric Association; 2000.
8. Akiskal HS. The bipolar spectrum—the shaping of a new paradigm in psychiatry. *Curr Psychiatry Rep*. 2002;4(1):1-3.
9. Akiskal HS, Pinto O. The evolving bipolar spectrum. Prototypes I, II, III, and IV. *Psychiatr Clin North Am*. 1999;22(3):517-534, vii.
10. Gunderson JC, Weinberg I, Daversa MT, et al. Descriptive and longitudinal observations on the relationship of borderline personality disorder and bipolar disorder. *Am J Psychiatry*. 2006;163(7):1173-1178.
11. Paris J, Gunderson J, Weinberg I. The interface between borderline personality disorder and bipolar spectrum disorders. *Compr Psychiatry*. 2007;48(2):145-154.
12. Paris J. Why psychiatrists are reluctant to diagnose: borderline personality disorder. *Psychiatry (Edgmont)*. 2007;4(1):35-39.
13. Paris J. Borderline or bipolar? Distinguishing borderline personality disorder from bipolar spectrum disorders. *Harv Rev Psychiatry*. 2004;12(3):140-145.
14. Ruggiero CJ, Zimmerman M, Chelminski I, et al. Borderline personality disorder and the misdiagnosis of bipolar disorder. *J Psychiatr Res*. 2010;44(6):405-408.
15. Zimmerman M. Problems diagnosing bipolar disorder in clinical practice. *Expert Rev Neurother*. 2010;10(7):1019-1021.
16. Stone MH. Relationship of borderline personality disorder and bipolar disorder. *Am J Psychiatry*. 2006;163(7):1126-1128.

Bottom Line

Although personality disorders can be difficult to diagnose—particularly in acute care settings—underdiagnosing or misdiagnosing borderline personality disorder (BPD) can have serious consequences, including delay in receiving effective treatment and adverse effects of unnecessary pharmacotherapy. Strategies for distinguishing BPD from bipolar disorder include a careful consideration of diagnostic criteria and differences in characteristic symptoms.

17. Gunderson JG. Clinical practice. Borderline personality disorder. *N Engl J Med*. 2011;364(21):2037-2042.
18. American Psychiatric Association. Practice guideline for the treatment of patients with borderline personality disorder. Washington, D.C.: American Psychiatric Association; 2001.
19. Paris J. The treatment of borderline personality disorder: implications of research on diagnosis, etiology, and outcome. *Annu Rev Clin Psychol*. 2009;5:277-290.
20. Stoffers J, Völm BA, Rucker G, et al. Pharmacological interventions for borderline personality disorder. *Cochrane Database Syst Rev*. 2010;(6):CD005653.
21. Ripoll LH, Triebwasser J, Siever LJ. Evidence-based pharmacotherapy for personality disorders. *Int J Neuropsychopharmacol*. 2011;14(9):1257-1288.
22. Mercer D, Douglass AB, Links PS. Meta-analyses of mood stabilizers, antidepressants and antipsychotics in the treatment of borderline personality disorder: effectiveness for depression and anger symptoms. *J Pers Disord*. 2009;23(2):156-174.
23. Lieb K, Völm B, Rucker G, et al. Pharmacotherapy for borderline personality disorder: Cochrane systematic review of randomised trials. *Br J Psychiatry*. 2010;196(1):4-12.
24. Links PS, Steiner M, Boiago I, et al. Lithium therapy for borderline patients: preliminary findings. *J Pers Disord*. 1990;4(2):173-181.
25. Goodman M, Roiff T, Oakes AH, et al. Suicidal risk and management in borderline personality disorder. *Curr Psychiatry Rep*. 2012;14(1):79-85.

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