

# soft

# BIPOLARITY

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# How to recognize and treat bipolar II disorder

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More realistic  
criteria for hypomania  
point to bipolarity in  
apparently unipolar  
depression

At least 25% and possibly up to 50% of patients with recurrent major depressive disorder (MDD) have features of mild hypomania (the “soft end” of the bipolar spectrum<sup>1</sup>) and might be better conceptualized as suffering from a broadly defined bipolar (BP) II disorder.<sup>2</sup> The challenge is to differentiate MDD from BP II so that we make treatment decisions—such as antidepressants vs mood stabilizers—shown to improve the long-term course of patients’ depressive symptoms.

Diagnosis of BP II often is not straightforward and unfortunately may be delayed several years after patients first present for evaluation. To help clinicians make correct diagnostic decisions, this article:

- describes diagnostic criteria outside of DSM-IV-TR that can assist in identifying BP II disorder
- identifies subgroups of recurrently depressed patients whose primary disorder is more likely to be bipolar than unipolar
- provides a screening tool validated for identifying “soft” bipolarity
- offers a pragmatic clinical perspective on the treatment of BP II disorder.

## How common is BP II disorder?

As with all psychiatric diagnoses, the prevalence of BP II disorder is a function of the diagnostic criteria used to define it.<sup>3</sup> BP II—1 or more depressive episodes with at least 1 hypomanic episode—affects 1% to 2% of the population, based on DSM-IV-TR criteria for hypomania (*Box 1, page 42*). However, the DSM definition of BP II



## Bipolar II

### Clinical Point

Instead of DSM's 4-day threshold, at least 1 day's duration would be a more realistic definition of hypomania in BP II disorder

### Box 1

## DSM-IV-TR criteria for a hypomanic episode

- A.** A distinct period of persistently elevated, expansive, or irritable mood, lasting at least 4 days, that is clearly different from the usual nondepressed mood
- B.** During the period of mood disturbance, 3 or more of the following symptoms have persisted (4 if the mood is only irritable) and have been present to a significant degree:
- 1) inflated self-esteem or grandiosity
  - 2) decreased need for sleep
  - 3) more talkative than usual or pressure to keep talking
  - 4) flight of ideas or subjective experience that thoughts are racing
  - 5) distractibility
  - 6) increase in goal-directed activity or psychomotor agitation
  - 7) excessive involvement in pleasurable activities that have potential for painful consequences
- C.** The episode is associated with an unequivocal change in functioning that is uncharacteristic of the person when not symptomatic
- D.** The disturbance in mood and the change in functioning are observable by others
- E.** The episode is not severe enough to cause marked impairment in social or occupational functioning, or to necessitate hospitalization, and there are no psychotic features
- F.** The symptoms are not due to the direct physiological effects of a substance (a drug of abuse, a medication, or other treatment) or a general medical condition (such as hyperthyroidism)

**Note:** Hypomanic-like episodes that are clearly caused by somatic antidepressant treatment (such as medication, electroconvulsive therapy, or light therapy) should not count toward a diagnosis of bipolar II disorder

might be too restrictive. Regarding the diagnosis of hypomania, in particular:

- the symptom of "overactivity" should be given as much weight as the stem criteria of "euphoria" and "irritability"
- the 4-day threshold for a hypomanic episode probably is too long.

The fact that DSM-IV-TR does not associate hypomania with marked functional impairment is somewhat counterintuitive. Most clinicians would agree that functional

### Table 1

## Proposed hypomania criteria in broadly defined BP II

- A.** Euphoria, irritability, or overactivity
- B.** At least 3 of the 7 DSM-IV-TR symptoms of hypomania
- C.** Hypomanic symptoms of at least 1 day's duration
- D.** Experience of negative consequences of hypomanic periods

BP II: bipolar II disorder  
Source: Reference 4

impairment is a useful criterion for clinical diagnosis of any psychiatric syndrome.

These deficiencies in DSM-IV-TR exclude many patients who experience brief but clinically significant periods of hypomania. A more realistic definition of hypomania within BP II disorder would:

- include overactivity as an additional stem criterion
- specify a threshold duration for hypomanic symptoms of at least 1 day rather than 4 days
- stipulate the experience of negative consequences of the episode as necessary for the diagnosis (*Table 1*).

In long-term follow-up studies of several thousand individuals, Angst et al<sup>4</sup> demonstrated that this definition of hypomania is clinically valid in terms of bipolar family history, treatment response, illness course, and clinical characteristics. When this broader definition of hypomania is used, population prevalence estimates for BP II rise from 1% to 2% to at least 5%.<sup>5</sup>

## Depression's subgroups

Recurrent MDD is an extremely heterogeneous diagnosis. It includes many clinical presentations of depressive illness that may share little in terms of etiology, pathophysiology, and response to treatment. When carefully assessed, 2 subgroups of recurrently depressed patients in particular appear to be more likely to have a primary bipolar disorder:

- young patients with early-onset severe depression

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## Bipolar II

### Clinical Point

Because patient insight regarding hypomania is poor, I find it enormously helpful to obtain a corroborative history from a relative

### Table 2 Possible indicators of bipolarity in apparently unipolar depression

Atypical features
First-degree relative with bipolar disorder
Antidepressant-induced mania or hypomania
Multiple family members with major depression
Early onset of depression (age <25)
Lack of response to $\geq 3$ antidepressant trials
Psychotic features (before age 35)
Mixed depressive episodes
Brief but frequent episodes of depression
Complex comorbidity (anxiety disorders, drug and alcohol misuse, previous diagnosis of borderline personality disorder)
Source: References 2,13,14

- older adults with difficult-to-treat or treatment-resistant depression.

A 15-year follow-up of young adults hospitalized with unipolar depression found that 27% subsequently developed hypomania and an additional 19% experienced at least 1 episode of mania.<sup>6</sup> Other reports have indicated that at least 40% of young adults with recurrent MDD satisfy broad diagnostic criteria for bipolar disorder.<sup>7</sup>

Higher rates of unrecognized bipolar disorder have been identified in patients with treatment-resistant depression. In a prospective study of 61 consecutive MDD patients referred to a mood disorders clinic, 59% satisfied DSM-IV-TR criteria for bipolar disorder.<sup>8</sup>

**Consequences.** Undiagnosed BP II disorder is an important clinical issue because bipolar features in patients presumed to have recurrent MDD can adversely affect long-term outcomes. Many of these patients will be treated exclusively with antidepressants despite evidence that antidepressant monotherapy for bipolar depression—at least for some patients—can cause more frequent mood episodes, mood destabilization, and possibly an increase in suicidal behaviors.<sup>9,10</sup>

This point is highlighted in the United

Kingdom's National Institute of Health and Clinical Excellence (NICE) guidelines for bipolar disorder, which recommended that antidepressants be prescribed for bipolar depression only in combination with mood stabilizer treatment and withdrawn within 2 to 3 months of recovery.<sup>11</sup>

The American Psychiatric Association's (APA) practice guideline for treating bipolar disorder, published in 2002, advises against antidepressants as monotherapy for bipolar depression, recommending instead that lithium or lamotrigine be used first-line. A revised APA guideline is scheduled for publication this year.<sup>12</sup>

### Why is BP II underdiagnosed?

Notwithstanding the limitations of DSM-IV-TR criteria for hypomania, additional factors contribute to under-recognition of BP II in clinical practice.

**Patient insight** regarding hypomania is generally poor. Not surprisingly, individuals with severe and disabling depressive episodes often fail to recognize the pathological aspects of brief (and comparatively infrequent) periods of elevated mood and overactivity. For this reason, I always obtain a corroborative history from a relative when assessing a patient for possible bipolar disorder. I find this enormously helpful for confirming or excluding a BP II diagnosis.

**Dominant depressive symptoms.** The clinical course of bipolar disorders is dominated by low-grade depressive symptoms and recurrent depressive episodes rather than mania or hypomania. This is especially true for BP II disorder, where the ratio of time spent with depressive symptoms relative to time with hypomanic symptoms is approximately 30:1.<sup>13</sup> The fact that BP II patients in general seek help only during depressive periods means that consultations inevitably focus on the diagnosis and treatment of depression, rather than long-term prophylaxis of both depressive and hypomanic episodes.

**Indistinguishable symptoms?** Bipolar depressions are generally thought to be

clinically indistinguishable from unipolar depressions, but this might not be clear-cut. Although differentiating symptoms of unipolar and bipolar depression can be difficult in clinical practice, evidence suggests that certain symptoms may be more common in bipolar than unipolar depression:

- atypical depressive features such as mood reactivity, overeating, oversleeping, and excessive fatigue<sup>14</sup>
- depressive psychotic symptoms, especially in younger patients<sup>15</sup>
- “mixed” depressive episodes (depressive episodes with concurrent manic symptoms).<sup>16</sup>

Other variables are associated with bipolar outcome in apparently unipolar depression (*Table 2*). These include shorter but more frequent depressive episodes and a strong family history for mood disorders, such as a first-degree relative with bipolar disorder or multiple family members with MDD. BP II also tends to be highly comorbid with anxiety disorders, alcohol and drug abuse, and personality disorders (especially borderline personality disorder).

### How to recognize BP II disorder

To detect and diagnose BP II disorder, systematically assess hypomanic features in all patients who present with recurrent MDD, especially those who have an early age of onset or don't seem to be responding well to antidepressant monotherapy. As noted, a corroborative history from a close relative is essential. Within a full clinical assessment, use the features listed in *Table 2* to help differentiate bipolar depression from unipolar depression.

**Screening instruments** for hypomania are no substitute for a careful psychiatric history but can be very helpful in everyday clinical practice. The most well-known is the Mood Disorder Questionnaire (MDQ);<sup>17</sup> other options include the Hypomania Checklist (HCL-32)<sup>18</sup> and the Bipolar Spectrum Diagnostic Scale (BSDS).<sup>19</sup> In general, the MDQ performs better at detecting BP I in psychiatric practice settings, whereas the HCL-32 and BSDS may be more useful in primary care and general population settings.<sup>20</sup>

The BSDS has a particular focus on the softer end of the bipolar spectrum,<sup>19</sup> and in my experience patients like its narrative structure. It can help prompt discussions about previous hypomania symptoms and mood instability. In this sense, the BSDS is a useful adjunct to the routine clinical assessment of



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## Bipolar II

### Clinical Point

Lithium remains a gold-standard treatment for BP II disorder; quetiapine or lamotrigine may be helpful for acute BP II depression

### Table 3 Recommendations for treating patients with BP II disorder

Most BP II patients require a multimodal team approach
Look for and treat psychiatric comorbidities, such as alcohol abuse
Lithium remains a gold standard treatment for BP II disorder
Quetiapine or lamotrigine may be helpful for acute bipolar II depression
Avoid antidepressant monotherapy for bipolar depression; some patients should avoid antidepressants altogether
CBT and IPSRT are useful psychological interventions
Family-focused and group psychoeducation are helpful in the long term
Always tailor treatments to the individual
BP II: bipolar II disorder; CBT: cognitive-behavioral therapy; IPSRT: interpersonal and social rhythm therapy

patients with recurrent depressive disorders. To view the BSDS, see this article at [CurrentPsychiatry.com](http://CurrentPsychiatry.com).

### Treatment strategies for BP II

As with all psychiatric disorders, treatment needs to be multimodal and tailored to the individual. For a detailed assessment of pharmacologic and psychological options, see Goodwin and Jamison's authoritative text, chapters 17 to 20.<sup>21</sup>

**Pharmacologic options.** Because few clinical trials have focused exclusively on BP II patients, much psychiatric practice has been extrapolated from trials involving BP I patients. Obviously, trials with BP II samples are needed, but these may be limited by the restrictive DSM-IV-TR definition of hypomania.

Lithium has the most supporting evidence, showing efficacy for all 3 phases of BP II—treatment of hypomania, treatment of bipolar depression, and prophylaxis against hypomanic and depressive relapses.<sup>22</sup> Different medications used in bipolar disorder appear to have different efficacy profiles, however. For example, a

systematic review of 14 randomized controlled trials with 2,526 patients found that although lithium, lamotrigine, olanzapine, and valproate were more effective than placebo at preventing relapse due to any mood episode:

- only lithium and olanzapine significantly reduced manic relapses
- only lamotrigine and valproate significantly reduced depressive relapses.<sup>23</sup>

Most guidelines warn against antidepressant monotherapy for bipolar depression, but uncertainty and debate surround antidepressants' effectiveness and risks (in terms of switching to mania or hypomania) when prescribed alongside mood stabilizers for bipolar depressive episodes.<sup>10,24</sup> In a study of nearly 600 patients with recurrent MDD, we found that those with a history of subthreshold manic symptoms were significantly more likely than those without manic features to respond poorly to antidepressants ( $P < .02$ , odds ratio 2.84). They also tended to have a much more morbid clinical course in terms of number and severity of depressive episodes.<sup>25</sup>

The Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) trial did not find any therapeutic benefit or increased risk of switching to mania for antidepressants plus mood stabilizer vs mood stabilizer alone.<sup>26</sup> Many trials of bipolar depression have recruited such heterogeneous groups of patients (including BP I, BP II, and BP NOS; schizoaffective disorder, bipolar type; and even recurrent MDD) that it is difficult to make firm recommendations about pharmacologic options for the depressive phase of BP II disorder.

In my experience, approximately one-third of BP II patients have a history of poor response to antidepressants or adverse effects from antidepressants (extreme irritability, activation, and antidepressant-induced hypomania). In the long term, these patients often do much better on mood stabilizer monotherapy or a combination of mood stabilizers such as lithium plus lamotrigine. The key is to be flexible with treatment options within recommended guidelines and to tailor treat-

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ment choices to the individual's pattern of illness and treatment preferences.

Placebo-controlled evidence supports the short-term (8 weeks) treatment of BP II depression with quetiapine monotherapy.<sup>27</sup> A recent systematic review and meta-analysis of individual patient data from randomized, controlled trials comparing lamotrigine with placebo found that lamotrigine has a modest beneficial effect on depressive symptoms in the depressed phase of bipolar disorder.<sup>28</sup>

**Psychological interventions.** Some evidence supports cognitive-behavioral therapy (CBT) and interpersonal and social rhythm therapy (IPSRT) in long-term treatment of bipolar disorders, although—as with medication trials—we need to be careful about extrapolating these findings to BP II disorder.<sup>29</sup> For example, a recent large-scale randomized controlled trial of CBT for bipolar disorder was largely negative.<sup>30</sup> Psychoeducation given in families and groups can be effective long-term options when used as adjuncts to medications.<sup>31</sup>

**Managing comorbidities.** BP II tends to be a complex, highly comorbid disorder that requires a coordinated, multifaceted approach. Unfortunately, we know little about which combinations of pharmacologic and nonpharmacologic interventions are most beneficial for BP II patients with comorbidities such as alcohol abuse. For this reason, optimal long-term management of the BP II patient requires a high degree of skill, flexibility, and coordination within the treating clinical team (*Table 3*).

## Related Resources

- Goodwin GM and the Consensus Group of the British Association for Psychopharmacology. Evidence-based guidelines for treating bipolar disorder: revised second edition—recommendations from the British Association for Psychopharmacology. *J Psychopharmacol.* 2009;23(4):346-388. [www.bap.org.uk/pdfs/Bipolar\\_guidelines.pdf](http://www.bap.org.uk/pdfs/Bipolar_guidelines.pdf).
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### Drug Brand Names

Lamotrigine • Lamictal	Quetiapine • Seroquel
Lithium • Various	Valproate • Depakon
Olanzapine • Zyprexa	

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## Clinical Point

Psychoeducation given in families and groups can be an effective long-term option as an adjunct to medications for BP II disorder

## Bottom Line

To detect bipolar II disorder, assess hypomanic features in all patients who present with recurrent major depressive symptoms. As a screening tool, the Bipolar Spectrum Diagnostic Scale has a particular focus on the softer end of the bipolar spectrum. Very little evidence exists to guide pharmacologic treatment of bipolar II disorder. The key is to be flexible within recommended guidelines, and tailor treatment choices to the individual's pattern of illness and treatment preferences.

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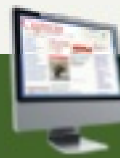
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# This month's instant poll



Ms. K, age 20, presents with a 4-month history of feeling severely depressed and irritable with racing thoughts, excessive daytime fatigue, overeating, weight gain, and hypersomnia. She describes 3 previous episodes starting at age 14 when she would suddenly become euphoric, overactive, and "full of plans and ideas." These episodes lasted less than 2 days and did not cause any functional impairment. Her mother has bipolar disorder. **What approach would you take?**

- Start an antidepressant such as a selective serotonin reuptake inhibitor and carefully monitor for emerging mania symptoms
- Administer a mood stabilizer such as lithium, lamotrigine, or quetiapine
- Treat her with a combination of an antidepressant and a mood stabilizer.
- Avoid medications for now and treat Ms. K with cognitive-behavioral therapy

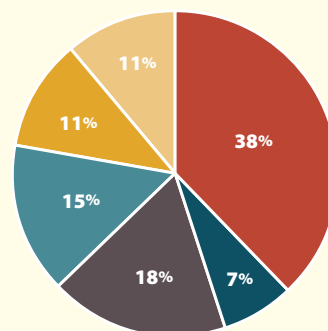


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## MAY POLL RESULTS

Mr. B, age 44, reports he is worried, can't sleep, and "feels depressed" after being laid off from his sales job at an auto dealership, where he had worked for 8 years. He presents with insomnia but does not meet criteria for major depressive disorder. **How would you treat him?**



- 38%** Cognitive-behavioral therapy (CBT)
- 7%** Antidepressant medication
- 18%** CBT plus antidepressant medication
- 15%** Exercise
- 11%** Advise Mr. B to stay positive and look for another sales position
- 11%** Other therapy

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