

## AN INTRODUCTION TO BIPOLAR DISORDER AND CO-OCCURRING SUBSTANCE USE DISORDERS

Bipolar disorder is a serious, chronic mental illness characterized by unusual changes in mood, energy, and activity levels. Early diagnosis and appropriate treatment of bipolar disorder are important because the illness carries a high risk of suicide and can severely impair academic and work performance, social and family relationships, and quality of life.<sup>1,2</sup>

Research suggests that from 30 percent<sup>3</sup> to more than 50 percent<sup>4,5,6,7,8</sup> of people with bipolar disorder (bipolar I or bipolar II) will develop a substance use disorder (SUD) sometime during their lives. This co-occurrence complicates the course, diagnosis, and treatment of SUDs. However, treatment for bipolar disorder and SUDs is available, and remission and recovery are possible—especially with early intervention.<sup>9,10,11</sup>

This *Advisory* provides behavioral health professionals with information on the symptoms of bipolar disorder and the potential complications of co-occurring bipolar disorder and SUDs. Readers will also learn about screening for bipolar disorder, challenges in diagnosing it, theories about its co-occurrence with SUDs, and research on treatment for these co-occurring conditions. Although treatment for bipolar disorder is highly individualized and therefore beyond the scope of this *Advisory*, a brief overview is included to provide basic information.

### An Overview of Bipolar Disorder

The *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, Text Revision (DSM-IV-TR),<sup>12</sup> classified bipolar disorder as a *mood disorder*, along with other related mood disorders (e.g., major depressive disorder, dysthymia).

However, the Fifth Edition (DSM-5)<sup>4</sup> placed bipolar disorder in a new category—“Bipolar and Related Disorders.”

Bipolar disorder involves experiencing two divergent emotional states: mania and depression, from which the disorder got its former name of *manic-depressive illness*. During manic episodes, people feel excited, self-confident, energetic, and euphoric, and often have a decreased need for sleep. During depressive episodes, they feel sad, despondent, and listless.

However, bipolar disorder is more complicated than a simple division between mania and depression. Many people with bipolar disorder go through periods when their mood is balanced, or *euthymic* (i.e., not euphoric, manic, or depressed), even without medication. Some people experience a “mixed state” that combines the features of mania and depression at the same time. Mania does not always involve feeling good, however. Some people feel irritable instead, especially when substance use is involved. Also, manic episodes can vary in severity. DSM-5 divides manic episodes into two types:

- **Mania**—Lasting at least a week and causing significant impairment in social and occupational functioning or requiring hospitalization
- **Hypomania**—Lasting at least 4 days, often with less severity (i.e., the change may be noticeable but may not impair functioning)

Some people with bipolar disorder experience psychotic features, such as delusions and hallucinations.

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Estimates of the lifetime prevalence of bipolar disorder in the United States range from 1 percent<sup>13</sup> to almost 4 percent.<sup>14\*</sup> Estimates for 12-month prevalence range from less than 1 percent<sup>4,13</sup> to 2.6 percent.<sup>15</sup> An analysis by Kessler, Petukhova, Sampson, Zaslavsky, and Wittchen<sup>16</sup> estimated the projected lifetime risk of developing bipolar disorder (in the United States) to be 4.1 percent.

One study found that individuals with bipolar disorder reported a significantly greater incidence of childhood trauma (such as sexual abuse or physical neglect) and internalized shame compared with a control group without bipolar disorder.<sup>17</sup> Another study found a history of childhood trauma in approximately 50 percent of individuals with bipolar disorder, and multiple forms of abuse were present in approximately 33 percent of individuals with bipolar disorder.<sup>18</sup> Other studies have also found an association between childhood trauma and a more complex or severe course of bipolar disorder.<sup>18,19</sup>

## The types of bipolar disorder

DSM-5 organizes bipolar disorder into several different diagnostic categories based, in large part, on the frequency and severity of the manic and depressive episodes. To be diagnosed with bipolar I disorder, an individual must have had at least one episode of mania. People with bipolar I disorder experience depression, but having a major depressive episode is not necessary for the diagnosis.<sup>4</sup>

The diagnostic criteria for bipolar II disorder include having at least one episode of hypomania that lasts at least 4 days and a major depressive episode that lasts at least 2 weeks. Between 5 and 15 percent of people with bipolar II disorder eventually have a manic episode that reclassifies their condition as bipolar I disorder.<sup>4</sup>

Bipolar II disorder is sometimes misunderstood as being less severe than bipolar I disorder. It is not. Like bipolar I, bipolar II is a chronic illness, and the depressive phases of bipolar II can be severe and disabling.<sup>4,20,21</sup>

\*The disparity between these estimates may be the result of algorithmic or other methodological differences.<sup>28</sup>

Significant numbers of individuals have bipolar symptoms at *subthreshold* or *subsyndromal* levels (i.e., below levels required for a diagnosis of bipolar I or II).<sup>22,23</sup> Some researchers have suggested that subthreshold bipolar symptom presentations be included in a broader category called *bipolar spectrum disorders*,<sup>22</sup> which could also include other types of bipolar disorders identified in DSM-5, such as cyclothymic disorder and substance/medication-induced bipolar and related disorder. The core patterns of bipolar disorder are illustrated in Exhibit 1.

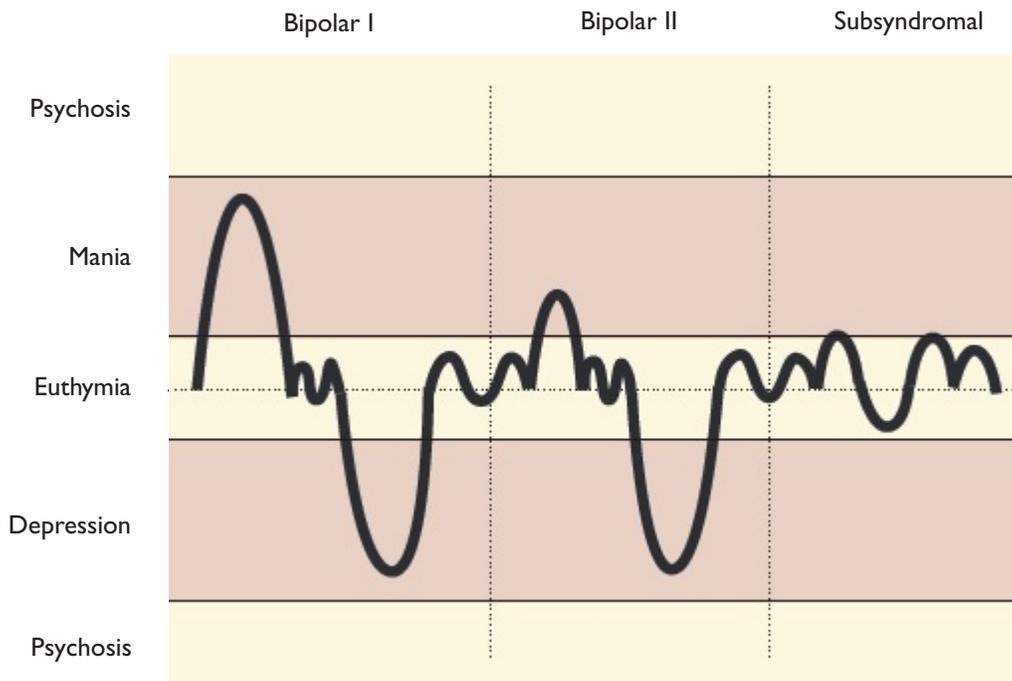
## Challenges of Diagnosing Bipolar Disorder

Some research suggests that bipolar disorder is underdiagnosed. One reason for underdiagnosis may be that people with bipolar disorder tend to seek treatment during a depressive phase, when manic or hypomanic episodes (or subthreshold symptoms) may not be readily remembered or may remain undetected by a clinician.<sup>24,25</sup> If providers do not elicit information from depressed patients about past episodes of mania and hypomania, these patients may be diagnosed with unipolar depression instead of bipolar disorder.

However, there is also evidence that bipolar disorder is overdiagnosed. A study of psychiatric outpatients found that less than half of those diagnosed with bipolar disorder actually had the disorder when researchers assessed them using the Structured Clinical Interview for DSM-IV.<sup>26</sup>

Other mental disorders can also be mistakenly diagnosed as bipolar disorder because of symptoms that overlap. For example, one study found that 40 percent of people with borderline personality disorder had been misdiagnosed as having bipolar disorder.<sup>27</sup> Bipolar disorder and attention deficit hyperactivity disorder also have many symptoms in common,<sup>4</sup> and distinguishing between the two is a task for an experienced, licensed mental health professional.

## Exhibit 1. The Core Patterns of Bipolar Disorder<sup>29</sup>



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Symptoms that appear to be caused by bipolar disorder may instead be symptoms of acute substance misuse or withdrawal. Chronic use of central nervous system stimulants, such as cocaine and amphetamines, can produce manic-like symptoms, including euphoria, increased energy, grandiosity, and paranoia, whereas withdrawal can produce

depression-like symptoms, including apathy, *anhedonia* (inability to feel pleasure), and thoughts of suicide. Chronic use of central nervous system depressants, such as alcohol, benzodiazepines, and opioids, can result in poor concentration, anhedonia, and sleep problems, whereas withdrawal can make people agitated and anxious.<sup>30</sup>

### The Difficulties of Diagnosing Bipolar Disorder in Children and Adolescents

Although the onset of bipolar disorder can occur at any age, the average age of onset for bipolar I is 18.<sup>4</sup> However, diagnosing bipolar disorder in children and adolescents can be even more difficult than diagnosing it in adults, in part because of the affective shifts that often occur in normal child and adolescent cognitive and emotional development.<sup>4,31</sup>

For more information, see:

**American Academy of Child and Adolescent Psychiatry, Bipolar Disorder Resource Center**

[www.aacap.org/AACAP/Families\\_and\\_Youth/Resource\\_Centers/Bipolar\\_Disorder\\_Resource\\_Center/Home.aspx](http://www.aacap.org/AACAP/Families_and_Youth/Resource_Centers/Bipolar_Disorder_Resource_Center/Home.aspx)

**National Institute of Mental Health, Bipolar Disorder in Children and Teens**

[www.nimh.nih.gov/health/publications/bipolar-disorder-in-children-and-teens-qf-15-6380/index.shtml](http://www.nimh.nih.gov/health/publications/bipolar-disorder-in-children-and-teens-qf-15-6380/index.shtml)

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It is important that a diagnosis of bipolar disorder be made by a mental health professional licensed to diagnose mental disorders and familiar with *differential diagnosis* (the process of distinguishing between illnesses or disorders with similar characteristics).

## Bipolar Disorder and Co-Occurring SUDs

Results from the National Epidemiologic Survey on Alcohol and Related Conditions showed that SUD co-occurrence was higher among people with bipolar disorder than among people with any of the other mental disorders included in the survey.<sup>32</sup> Studies indicate that lifetime co-occurrence of SUDs for individuals with bipolar disorder ranges from 21.7 percent<sup>33</sup> to 59 percent<sup>34</sup> and that 12-month co-occurrence ranges from 4 percent<sup>35</sup> to more than 25 percent.<sup>32</sup> However, it is not only individuals meeting full criteria for bipolar disorder who are at risk for SUDs. Hypomania is also associated with an increased risk for SUDs.<sup>36</sup>

Alcohol is commonly misused by people with bipolar disorder,<sup>6,34,35</sup> and people with bipolar disorder and co-occurring alcohol use disorder are less likely to respond and adhere to treatment and more likely to be hospitalized<sup>34</sup> and to attempt suicide<sup>37,38</sup> than people with bipolar disorder only. In some cases, the combination of bipolar disorder and an SUD may deepen bipolar disorder's manic and depressive symptoms.<sup>34,39,40</sup>

## Explanations for bipolar disorder and SUDs co-occurrence

Researchers have offered several possible explanations for bipolar disorder and SUD co-occurrence. Khantzian<sup>41</sup> formulated the self-medication hypothesis, which proposes that people misuse substances to relieve psychological suffering and that the substances they misuse are specific to the type of suffering they experience.

Swann<sup>42</sup> argues that bipolar disorder and substance misuse can be viewed as overlapping disorders of the systems in the brain that regulate impulsivity, motivation, and the feeling of reward. Another model for co-occurring bipolar disorder and SUDs proposes an underlying shared vulnerability (e.g., genetic liability).<sup>43,44</sup> Whatever the etiology, it is clear that SUDs may precede, precipitate, exacerbate, be a consequence of, or have separate etiologies from bipolar disorder,<sup>40,45</sup> and the co-occurrence of bipolar disorder and SUDs can complicate both diagnosis and treatment.<sup>33,34,40,45</sup>

## Screening for Bipolar Disorder

Because bipolar disorder has a wide range of symptoms, it can be mistaken for other conditions. This can make screening (and diagnosis) difficult. Substance use treatment professionals using screening tools for mental disorders should remember that these tools are not for *diagnosis*. Clients who screen positive for bipolar disorder—or, in fact, *any* mental disorder—will need to be referred for an assessment by a behavioral health professional licensed to diagnose and treat mental disorders. The same is true for clients who are not formally screened but who appear to have mental disorders.

One well-known screening tool for bipolar disorder is the Composite International Diagnostic Interview (CIDI)-Based Screening Scale for Bipolar Spectrum Disorders. The CIDI-based screening scale consists of questions about symptom clusters and individual symptoms. Researchers have estimated that the

For more information about general screening for mental disorders, see Treatment Improvement Protocol (TIP) 42, *Substance Abuse Treatment for Persons With Co-Occurring Disorders*.<sup>46</sup>

CIDI-based screening scale identifies between 67 percent and 96 percent of bipolar disorder cases, depending in part on where the cut points for a positive result are set.<sup>47</sup> The screening scale is available at [www.integration.samhsa.gov/images/res/STABLE\\_toolkit.pdf](http://www.integration.samhsa.gov/images/res/STABLE_toolkit.pdf).

## A Brief Overview of Bipolar Disorder Treatment

Only a behavioral health professional who is licensed to diagnose and treat mental disorders should provide treatment for bipolar disorder. Treatment can be complex and is often individualized according to a patient's symptoms, needs, preferences, and responses to treatment. Treatment generally involves both pharmacological and psychosocial therapies, as described below.

### Pharmacological therapy

- **Mood stabilizers**—Lithium has been the first-line mood stabilizer for years, but other mood stabilizers, such as divalproex sodium (Depakote) and several other anticonvulsants, are also often prescribed.<sup>48,49,50</sup>
- **Atypical antipsychotics**—Atypical (or “second generation”) antipsychotics such as quetiapine (Seroquel) or olanzapine (Zyprexa) are often used alone or in combination with other medications, such as lithium.<sup>49,50</sup> In 2013, the Food and Drug Administration (FDA) approved the atypical antipsychotic lurasidone (Latuda) for the treatment of bipolar depression, alone or in combination with lithium or valproate.<sup>51</sup> Atypical antipsychotics are not only used when psychotic symptoms are present. Many are used to treat mania; only one medication (quetiapine) is indicated for treatment of both bipolar mania and depression.<sup>49,50</sup>
- **Antidepressants**—There is no FDA-approved antidepressant monotherapy for bipolar disorder. The selective serotonin reuptake inhibitor (SSRI) fluoxetine (Prozac), in combination

with the atypical antipsychotic olanzapine, is approved for acute bipolar I depression;<sup>52</sup> the fluoxetine–olanzapine combination is available in a single capsule (Symbyax). Other SSRIs are also sometimes used (off label) for depressive episodes—but typically in conjunction with a mood stabilizer, because of concerns that antidepressant monotherapy could precipitate a manic or hypomanic episode.<sup>49,50</sup>

Each of these types of medications has its own potential side effects (such as weight gain with some atypical antipsychotics) or contraindications (e.g., divalproex sodium is contraindicated in pregnant women).<sup>48,49</sup> Combining these medications with alcohol or drugs can be quite dangerous. For example, marijuana can cause a dramatic and even toxic increase in lithium levels.<sup>53</sup> Mixing alcohol with atypical antipsychotics may result in an extreme level of central nervous system depression and significantly impair psychomotor functioning.<sup>54</sup>

### Psychosocial therapy

- **Cognitive–behavioral therapy (CBT)**—CBT uses a process called *cognitive restructuring*, in which an individual learns to identify harmful or negative patterns of thoughts, behaviors, and beliefs and to modify them into more balanced patterns. The goal is to decrease the individual's degree of emotional distress over troubling situations.<sup>1,55</sup>
- **Family-focused therapy (FFT)**—FFT helps families understand bipolar disorder, develop coping strategies, and learn to recognize when a new depressive or manic/hypomanic episode may be beginning. FFT also focuses on improving family communication and problem-solving skills.<sup>1</sup>
- **Interpersonal and social rhythm therapy (IPSRT)**—IPSRT has three components:<sup>56</sup>
  - *Psychoeducation* focuses on information about bipolar disorder, treatment options (and possible side effects), and early warning signs of a new depressive or manic/hypomanic episode.

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- *Social rhythm therapy* focuses on identifying situations that may upset life routines and developing ways to stabilize life routines, to reduce emotional distress.
- *Interpersonal psychotherapy* focuses on the ways that interpersonal problems (such as grief, role transitions, or disputes) may be related to changes in mood that may signal the beginning of new mood episodes, such as new or increased depression or mania/hypomania.

One study found that patients who received any one of these types of psychosocial treatment (CBT, FFT, or IPSRT) had higher levels of life satisfaction, better overall functioning, and better relationship functioning than patients who received a three-session psychoeducational intervention.<sup>57</sup>

BD [bipolar disorder] is a uniquely challenging disorder to treat, with the most lethality, the most recurrences, and the most varied clinical presentations of any major psychiatric disorder.<sup>58</sup>

## Treatment of Co-Occurring Bipolar Disorder and SUDs

Because SUDs are chronic and progressive illnesses and because SUDs (both past and current) tend to contribute to poorer treatment outcomes for individuals with bipolar disorder, early intervention can be an important part of improving treatment outcomes for individuals with co-occurring SUDs and bipolar disorder.<sup>59</sup>

Like treatment for bipolar disorder without a co-occurring SUD, treatment for co-occurring bipolar disorder and SUDs usually involves both pharmacological and psychosocial therapies.

## Pharmacological therapy

Many of the medications for bipolar disorder are also used to treat individuals with co-occurring bipolar disorder and SUDs, but there has been limited research on regimens that might be efficacious for both disorders simultaneously. One such study found that divalproex sodium, an anticonvulsant mood stabilizer often used to treat manic episodes, was associated with a reduction in alcohol consumption when used as a maintenance treatment with lithium.<sup>60</sup>

Quetiapine is one of the atypical antipsychotics often prescribed for bipolar disorder that has been studied for its possible efficacy for alcohol use disorder. Although some studies have found that quetiapine helped decrease alcohol consumption and craving,<sup>61,62</sup> other studies have had negative or inconsistent results.<sup>39,63,64,65</sup> However, a clinical synthesis<sup>66</sup> concluded that there appears to be no evidence for avoiding the use of medication-assisted treatment medications (especially for alcohol use disorder and opioid use disorder) in the treatment of individuals with co-occurring bipolar disorder and SUDs.

## Psychosocial therapy

Psychosocial therapy for co-occurring mental disorders and SUDs tends to involve three main treatment approaches: sequential, parallel, and integrated. With sequential treatment, providers tackle the more serious disorder first and, after that has been brought under control, then address the other disorder. In parallel treatment, the conditions are treated at the same time in different settings. Integrated treatment involves a provider or a team of providers addressing the disorders simultaneously.<sup>67</sup> However, integrated care is not simply simultaneously delivered interventions that have been developed for each individual disorder, as if co-occurring disorders were essentially unrelated to the physiology, emotions, and overall life of individuals.<sup>39</sup> Truly integrated treatment allows for the treatment of the whole person—including medical and medication issues, mental disorders, and SUD treatment as necessary

(see the Resources section for more information). In the absence of integrated treatment, collaboration between providers becomes even more important.

One type of integrated treatment uses a cognitive-behavioral relapse prevention model that also incorporates elements of individualized interpersonal therapy, the use of psychoeducational materials and group sessions, and involvement with mutual-help groups (such as Alcoholics Anonymous and Dual Recovery Anonymous).<sup>67</sup> Another model for integrated treatment follows basic principles that are represented by the acronym FIRESIDE (Exhibit 2).<sup>68</sup>

Proponents of a form of integrated treatment called Integrated Group Therapy (IGT) believe that clients with co-occurring bipolar disorder and SUDs should be encouraged to view co-occurrence as a single disorder—"bipolar substance abuse." Clients are also advised that substance use will worsen their bipolar disorder and that not taking bipolar medication will increase the risk of SUD relapse.<sup>67</sup>

One study found that the likelihood of achieving at least 1 month of abstinence during treatment was

almost twice as high for individuals who participated in IGT compared with individuals who participated in group drug counseling (71.0 percent and 40.0 percent, respectively), and IGT participants were almost three times as likely to remain abstinent during all 3 months of treatment when compared with individuals who participated in group drug counseling (35.5 percent and 13.3 percent, respectively).<sup>69</sup> In addition, the IGT participants were more than twice as likely to be both abstinent and free of mood episodes during the last month of treatment when compared with individuals who participated in group drug counseling (45.2 percent and 20.0 percent, respectively).

It is also important for clients and professionals to shift the focus from primarily illness and disease to wellness and recovery. An approach focusing on wellness and recovery is strengths based and includes interventions to help clients become proactive in managing their overall health and well-being.<sup>70</sup> It focuses on reclaiming important aspects of life that were lost when a mental or substance use disorder began, or on discovering these aspects for the first time. The Substance Abuse and Mental

## Exhibit 2. The FIRESIDE Principles for an Integrated Treatment of Bipolar Disorder and Alcohol Use Disorder<sup>68</sup>

- **F**ollow-up. The importance of aftercare strongly emphasized.
- **I**nterrelationship of diagnoses. Can't improve in one without treating the other.
- **R**elapse Prevention. The main addiction therapeutic intervention.
- **E**ducation. Use of lectures, videos, and discussions.
- **S**tabilization of withdrawal and mood. Pharmacotherapy used aggressively during and after the program.
- **I**ndividuation of program. Flexibility of program to aid retention.
- **D**iagnostic equivalence. Both diagnoses emphasized equally.
- **E**mpowerment. Individual responsibility encouraged and demanded.

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## Exhibit 3. Dimensions of Recovery and Dimensions of Wellness<sup>71,72,73</sup>

Dimensions of Recovery	Dimensions of Wellness
<b>Health</b>	<ul style="list-style-type: none"> <li>• <i>Physical</i>: Recognizing the need for physical activity, healthy foods, and sleep; managing chronic illnesses</li> <li>• <i>Emotional</i>: Coping effectively with life and creating satisfying relationships</li> </ul>
<b>Home</b>	<ul style="list-style-type: none"> <li>• <i>Environmental</i>: Occupying pleasant, safe, stimulating environments that support well-being</li> <li>• <i>Financial</i>: Obtaining satisfaction with current and future financial situations</li> </ul>
<b>Purpose</b>	<ul style="list-style-type: none"> <li>• <i>Intellectual</i>: Recognizing creative abilities and finding ways to expand knowledge and skills</li> <li>• <i>Occupational</i>: Obtaining personal satisfaction and enrichment from one's work or daily activity</li> <li>• <i>Spiritual</i>: Expanding one's sense of purpose and meaning in life</li> </ul>
<b>Community</b>	<ul style="list-style-type: none"> <li>• <i>Social</i>: Building a sense of connection and belonging; building a well-developed support system</li> </ul>

Health Services Administration has identified several essential dimensions of a holistic approach to recovery and wellness (see Exhibit 3).

### Conclusion

Bipolar disorder can be difficult to diagnose and treat. When bipolar disorder co-occurs with SUDs, the complexities only increase. These complexities reinforce the importance of collaboration between the medical and behavioral health services professionals who provide treatment to individuals with these co-occurring disorders. For example, clients may see behavioral health professionals more frequently than they see medical providers; consequently, behavioral health professionals may become aware first of new symptoms, medication side effects, or other problems requiring medical attention. Integrated treatment, collaboration between professionals and the client, and attention to the various aspects of recovery can all work together to facilitate the management of these co-occurring disorders.

### Resources

**Behavioral Health Treatment Services Locator**  
<https://findtreatment.samhsa.gov>

**Bipolar Network News**  
[www.bipolarnews.org](http://www.bipolarnews.org)

**Depression and Bipolar Support Alliance**  
[www.dbsalliance.org](http://www.dbsalliance.org)

**National Alliance on Mental Illness**  
[www.nami.org/Learn-More/Mental-Health-Conditions/Bipolar-Disorder](http://www.nami.org/Learn-More/Mental-Health-Conditions/Bipolar-Disorder)

**National Institute of Mental Health**  
[www.nimh.nih.gov/health/topics/bipolar-disorder](http://www.nimh.nih.gov/health/topics/bipolar-disorder)

**National Institute on Drug Abuse**  
[www.drugabuse.gov/news-events/nida-notes/2010/04/attention-to-bipolar-disorder-strengthens-substance-abuse-treatment](http://www.drugabuse.gov/news-events/nida-notes/2010/04/attention-to-bipolar-disorder-strengthens-substance-abuse-treatment)

**SAMHSA-HRSA Center for Integrated Health Solutions**  
[www.integration.samhsa.gov/integrated-care-models](http://www.integration.samhsa.gov/integrated-care-models)

## Notes

- <sup>1</sup> Miklowitz, D. J., & Johnson, S. L. (2006). The psychopathology and treatment of bipolar disorder. *Annual Review of Clinical Psychology, 2*, 199–235.
- <sup>2</sup> National Institute of Mental Health. (2015). *Bipolar Disorder*. NIH Publication No. TR 15-3679. Bethesda, MD: Author.
- <sup>3</sup> Lagerberg, T. V., Andreassen, O. A., Ringen, P. A., Berg, A. O., Larsson, S., Agartz, I., et al. (2010). Excessive substance use in bipolar disorder is associated with impaired functioning rather than clinical characteristics, a descriptive study. *BMC Psychiatry, 10*, 1–9. doi:10.1186/1471-244X-10-9
- <sup>4</sup> American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.
- <sup>5</sup> Bauer, M. S., Altshuler, L., Evans, D. R., Beresford, T., Williford, W. O., & Hauger, R., for the VA Cooperative Study #430 Team. (2005). Prevalence and distinct correlates of anxiety, substance, and combined comorbidity in a multi-site public sector sample with bipolar disorder. *Journal of Affective Disorders, 85*, 301–315.
- <sup>6</sup> Bizzarri, J. V., Sbrana, A., Rucci, P., Ravani, L., Massei, G. J., Gonnelli, C., et al. (2007). The spectrum of substance abuse in bipolar disorder: Reasons for use, sensation seeking and substance sensitivity. *Bipolar Disorders, 9*, 213–220.
- <sup>7</sup> Chengappa, K. N. R., Levine, J., Gershon, S., & Kupfer, D. J. (2000). Lifetime prevalence of substance or alcohol abuse and dependence among subjects with bipolar I and II disorders in a voluntary registry. *Bipolar Disorders, 2*, 191–195.
- <sup>8</sup> Regier, D. A., Farmer, M. E., Rae, D. S., Locke, B. Z., Keith, S. J., Judd, L. L., & Goodwin, F. K. (1990). Comorbidity of mental disorders with alcohol and other drug abuse: Results from the Epidemiologic Catchment Area (ECA) study. *JAMA, 264*(19), 2511–2518.
- <sup>9</sup> Drake, R. E., Xie, H., McHugo, G. J., & Shumway, M. (2004). Three-year outcomes of long-term patients with co-occurring bipolar and substance use disorders. *Biological Psychiatry, 56*, 749–756.
- <sup>10</sup> Gignac, A., McGirr, A., Lam, R. W., & Yatham, L. N. (2015). Course and outcome following a first episode of mania: Four-year prospective data from the Systematic Treatment Optimization Program (STOP-EM). *Journal of Affective Disorders, 175*, 411–417.
- <sup>11</sup> Vieta, E., Reinares, M., & Rosa, A. R. (2011). Staging bipolar disorder. *Neurotoxicity Research, 19*, 279–285.
- <sup>12</sup> American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text revision). Washington, DC: Author.
- <sup>13</sup> Merikangas, K. R., Jin, R., He, J.-P., Kessler, R. C., Lee, S., Sampson, N. A., et al. (2011). Prevalence and correlates of bipolar spectrum disorder in the World Mental Health Survey Initiative. *Archives of General Psychiatry, 68*(3), 241–251.
- <sup>14</sup> Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry, 62*(6), 593–602.
- <sup>15</sup> Kessler, R. C., Chiu, W. T., Demler, O., Merikangas, K. R., & Walters, E. E. (2005). Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication (NCSR). *Archives of General Psychiatry, 62*(6), 617–627.
- <sup>16</sup> Kessler, R. C., Petukhova, M., Sampson, N. A., Zaslavsky, A. M., & Wittchen, H.-U. (2012). Twelve-month and lifetime prevalence and lifetime morbid risk of anxiety and mood disorders in the United States. *International Journal of Methods in Psychiatric Research, 21*(3), 169–184.
- <sup>17</sup> Fowke, A., Ross, S., & Ashcroft, K. (2012). Childhood maltreatment and internalized shame in adults with a diagnosis of bipolar disorder. *Clinical Psychology and Psychotherapy, 19*, 450–457.
- <sup>18</sup> Garno, J. L., Goldberg, J. F., Ramirez, P. M., & Ritzler, B. A. (2005). Impact of childhood abuse on the clinical course of bipolar disorder. *British Journal of Psychiatry, 186*, 121–125.
- <sup>19</sup> Larsson, S., Aas, M., Klungsoyr, O., Agartz, I., Mork, E., Steen, N. E., et al. (2013). Patterns of childhood adverse events are associated with clinical characteristics of bipolar disorder. *BMC Psychiatry, 13*(97), 1–9. doi:10.1186/1471-244X-13-97
- <sup>20</sup> Judd, L. L., Akiskal, H. S., Schettler, P. J., Coryell, W., Endicott, J., Maser, J. D., et al. (2003). A prospective investigation of the natural history of the long-term weekly symptomatic status of bipolar II disorder. *Archives of General Psychiatry, 60*(3), 261–269.
- <sup>21</sup> Judd, L. L., Akiskal, H. S., Schettler, P. J., Endicott, J., Leon, A. C., Solomon, D. A., et al. (2005). Psychosocial disability in the course of bipolar I and II disorders: A prospective, comparative, longitudinal study. *Archives of General Psychiatry, 62*(12), 1322–1330.

- <sup>22</sup> Akiskal, H. S., Bourgeois, M. L., Angst, J., Post, R., Möller, H.-J., & Hirschfeld, R. (2000). Re-evaluating the prevalence of and diagnostic composition within the broad clinical spectrum of bipolar disorders. *Journal of Affective Disorders*, *59*, S5–S30.
- <sup>23</sup> Merikangas, K. R., Akiskal, H. S., Angst, J., Greenberg, P. E., Hirschfeld, R. M. A., Petukhova, M., & Kessler, R. C. (2007). Lifetime and 12-month prevalence of bipolar spectrum disorder in the National Comorbidity Survey Replication. *Archives of General Psychiatry*, *64*(5), 543–552.
- <sup>24</sup> Angst, J., Azorin, J.-M., Bowden, C. L., Perugi, G., Vieta, E., Gamma, A., & Young, A. H. (2011). Prevalence and characteristics of undiagnosed bipolar disorders in patients with a major depressive episode: The BRIDGE study. *Archives of General Psychiatry*, *68*(8), 791–799.
- <sup>25</sup> Zimmerman, M., Galione, J. N., Chelminski, I., Young, D., & Dalrymple, K. (2011). Psychiatric diagnoses in patients who screen positive on the Mood Disorder Questionnaire: Implications for using the scale as a case-finding instrument for bipolar disorder. *Psychiatry Research*, *185*, 444–449.
- <sup>26</sup> Zimmerman, M., Ruggero, C. J., Chelminski, I., & Young, D. (2008). Is bipolar disorder overdiagnosed? *Journal of Clinical Psychiatry*, *69*(6), 935–940.
- <sup>27</sup> Ruggero, C. J., Zimmerman, M., Chelminski, I., & Young, D. (2010). Borderline personality disorder and the misdiagnosis of bipolar disorder. *Journal of Psychiatric Research*, *44*(6), 405–408.
- <sup>28</sup> Mitchell, P. B., Johnston, A. K., Frankland, A., Slade, T., Green, M. J., Roberts, G., et al. (2013). Bipolar disorder in a national survey using the World Mental Health Version of the Composite International Diagnostic Interview: The impact of differing diagnostic algorithms. *Acta Psychiatrica Scandinavica*, *127*, 381–393.
- <sup>29</sup> Malhi, G. S., Adams, D., Lampe, L., Paton, M., O'Connor, N., Newton, L. A., et al. (2009). Clinical practice recommendations for bipolar disorder. *Acta Psychiatrica Scandinavica*, *119*(Suppl. 439), 27–46.
- <sup>30</sup> Quello, S. B., Brady, K. T., & Sonne, S. C. (2005). Mood disorders and substance use disorder: A complex comorbidity. *Science and Practice Perspectives*, *3*(1), 13–21.
- <sup>31</sup> Birmaher, B. (2013). Bipolar disorder in children and adolescents. *Child and Adolescent Mental Health*, *18*(3), 140–148.
- <sup>32</sup> Grant, B. F., Stinson, F. S., Dawson, D. A., Chou, P., Dufour, M. C., Compton, W., et al. (2004). Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Archives of General Psychiatry*, *61*, 807–816.
- <sup>33</sup> Ostacher, M. J., Perlis, R. H., Nierenberg, A. A., Calabrese, J., Stange, J. P., Salloum, I., et al. (2010). Impact of substance use disorders on recovery from episodes of depression in bipolar disorder patients: Prospective data from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). *American Journal of Psychiatry*, *167*(3), 289–297.
- <sup>34</sup> Cassidy, F., Ahearn, E. P., & Carroll, B. J. (2001). Substance abuse in bipolar disorder. *Bipolar Disorders*, *3*, 181–188.
- <sup>35</sup> McElroy, S. L., Altshuler, L. L., Suppes, T., Keck, P. E., Jr., Frye, M. A., Denicoff, K. D., et al. (2001). Axis I psychiatric comorbidity and its relationship to historical illness variables in 288 patients with bipolar disorder. *American Journal of Psychiatry*, *158*(3), 420–426.
- <sup>36</sup> Do, E. K., & Mezuk, B. (2013). Comorbidity between hypomania and substance use disorders. *Journal of Affective Disorders*, *150*, 974–980.
- <sup>37</sup> Dalton, E. J., Cate-Carter, T. D., Mundo, E., Parikh, S. V., & Kennedy, J. L. (2003). Suicide risk in bipolar patients: The role of co-morbid substance use disorders. *Bipolar Disorders*, *5*, 58–61.
- <sup>38</sup> Potash, J. B., Kane, H. S., Chiu, Y.-F., Simpson, S. G., MacKinnon, D. F., McInnis, M. G., et al. (2000). Attempted suicide and alcoholism in bipolar disorder: Clinical and familial relationships. *American Journal of Psychiatry*, *157*, 2048–2050.
- <sup>39</sup> Lavoie, S., & Levy, B. (2012). Available treatment for bipolar disorder with co-occurring substance and alcohol use disorders: A review. *Current Psychiatry Reviews*, *8*, 83–96.
- <sup>40</sup> Levin, F. R., & Hennessy, G. (2001). Bipolar disorder and substance abuse. *Biological Psychiatry*, *56*, 738–748.
- <sup>41</sup> Khantzian, E. J. (1985). The self-medication hypothesis of addictive disorders: Focus on heroin and cocaine dependence. *American Journal of Psychiatry*, *142*, 1259–1264.
- <sup>42</sup> Swann, A. C. (2010). The strong relationship between bipolar and substance-use disorder. *Annals of the New York Academy of Sciences*, *1187*, 276–293.
- <sup>43</sup> Alloy, L. B., Bender, R. E., Wagner, C. A., Whitehouse, W. G., Abramson, L. Y., Hogan, M. E., et al. (2009). Bipolar spectrum-substance use co-occurrence: Behavioral approach system (BAS) sensitivity and impulsiveness as shared personality vulnerabilities. *Journal of Personality and Social Psychology*, *97*(3), 549–565.
- <sup>44</sup> Martins, S. S., Fenton, M. C., Keyes, K. M., Blanco, C., Zhu, H., & Storr, C. L. (2012). Mood/anxiety disorders and their association with non-medical prescription opioid use and prescription opioid use disorder: Longitudinal evidence from the National Epidemiologic Study on Alcohol and Related Conditions. *Psychological Medicine*, *42*(6), 1261–1272.

- <sup>45</sup> Soone, S. C., & Brady, K. T. (2002). *Bipolar disorder and alcoholism* [Webpage]. National Institute on Alcohol Abuse and Alcoholism. Retrieved April 1, 2016, from <http://pubs.niaaa.nih.gov/publications/arh26-2/103-108.htm>
- <sup>46</sup> Substance Abuse and Mental Health Services Administration. (2005). *Substance abuse treatment for persons with co-occurring disorders*. Treatment Improvement Protocol (TIP) Series 42. HHS Publication No. (SMA) 13-3992. Rockville, MD: Substance Abuse and Mental Health Services Administration.
- <sup>47</sup> Kessler, R. C., Akiskal, H. S., Angst, J., Guyer, M., Hirschfeld, R. M. A., Merikangas, K. R., & Stang, P. E. (2006). Validity of the assessment of bipolar spectrum disorders in the WHO CIDI 3.0. *Journal of Affective Disorders*, *96*(3), 259–269.
- <sup>48</sup> Cipriani, A., Reid, K., Young, A. H., Macritchie, K., & Geddes, J. (2013). Valproic acid, valproate and divalproex in the maintenance treatment of bipolar disorder. *Cochrane Database of Systematic Reviews*, *2013*(10), i–73. doi:10.1002/14651858.CD003196.pub2
- <sup>49</sup> Connolly, K. R., & Thase, M. E. (2011). The clinical management of bipolar disorder: A review of evidence-based guidelines. *Primary Care Companion for CNS Disorders*, *13*(4). doi:10.4088/PCC.10r01097
- <sup>50</sup> Severus, E., Schaaff, N., & Möller, H.-J. (2012). State of the art: Treatment of bipolar disorders. *CNS Neuroscience and Therapeutics*, *18*, 214–218.
- <sup>51</sup> Sunovion Pharmaceuticals. (2013, July). *Latuda: Highlights of prescribing information*. Retrieved April 1, 2016, from [www.accessdata.fda.gov/drugsatfda\\_docs/label/2013/200603s015lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/200603s015lbl.pdf)
- <sup>52</sup> Eli Lilly. (2014, July). *Prozac: Highlights of prescribing information*. Retrieved April 1, 2016, from [www.accessdata.fda.gov/drugsatfda\\_docs/label/2014/018936s102lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/018936s102lbl.pdf)
- <sup>53</sup> Venkatakrisnan, K., Shader, R. I., & Greenblatt, D. J. (2006). Concepts and mechanisms of drug disposition and drug interactions. In D. A. Ciraulo, R. I. Shader, D. J. Greenblatt, & W. Creelman (Eds.), *Drug interactions in psychiatry* (3rd ed., pp. 1–46). Philadelphia, PA: Lippincott Williams & Wilkins.
- <sup>54</sup> Johnson, B. A., & Seneviratne, C. (2014). Alcohol–medical drug interactions. In M. J. Aminoff, F. Boller, & D. F. Swaab (Series Eds.), E. V. Sullivan & A. Pfefferbaum (Vol. Eds.), *Handbook of clinical neurology* (3rd series): *Vol. 125. Alcohol and the nervous system* (pp. 543–559). Waltham, MA: Elsevier.
- <sup>55</sup> Wenzel, A. (2013). *Strategic decision making in cognitive behavioral therapy*. Washington, DC: American Psychological Association.
- <sup>56</sup> Swartz, H. A., Levenson, J. C., & Frank, E. (2012). Psychotherapy for bipolar II disorder: The role of interpersonal and social rhythm therapy. *Professional Psychology: Research and Practice*, *43*(2), 145–153.
- <sup>57</sup> Miklowitz, D. J., Otto, M. W., Frank, E., Reilly-Harrington, N. A., Kogan, J. N., Sachs, G. S., et al. (2007). Intensive psychosocial intervention enhances functioning in patients with bipolar depression: Results from a 9-month randomized controlled trial. *American Journal of Psychiatry*, *164*(9), 1340–1347.
- <sup>58</sup> Parikh, S. V., LeBlanc, S. R., & Ovanessian, M. M. (2010). Advancing bipolar disorder: Key lessons from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) (p. 141). *Canadian Journal of Psychiatry*, *55*(3), 136–143.
- <sup>59</sup> Baethge, C., Baldessarini, R. J., Khalsa, H.-M. K., Hennen, J., Salvatore, P., & Tohen, M. (2005). Substance abuse in first-episode bipolar I disorder: Indications for early intervention. *American Journal of Psychiatry*, *162*, 1008–1010.
- <sup>60</sup> Salloum, I. M., Cornelius, J. R., Daley, D. C., Kirisci, L., Himmelhoch, J. M., & Thase, M. E. (2005). Efficacy of valproate maintenance in patients with bipolar disorder and alcoholism: A double-blind placebo-controlled study. *Archives of General Psychiatry*, *62*(1), 37–45.
- <sup>61</sup> Kampman, K. M., Pettinati, H. M., Lynch, K. G., Whittingham, T., Macfadden, W., Dackis, C., et al. (2007). A double-blind, placebo-controlled pilot trial of quetiapine for the treatment of Type A and Type B alcoholism. *Journal of Clinical Psychopharmacology*, *27*, 344–351.
- <sup>62</sup> Martinotti, G., Andreoli, S., Di Nicola, M., Di Giannantonio, M., Sarchiapone, M., & Janiri, L. (2008). Quetiapine decreases alcohol consumption, craving, and psychiatric symptoms in dually diagnosed alcoholics. *Human Psychopharmacology Clinical and Experimental*, *23*, 417–424.
- <sup>63</sup> Brown, E. S., Davila, D., Nakamura, A., Carmody, T. J., Rush, A. J., Lo, A., et al. (2014). A randomized, double-blind, placebo-controlled trial of quetiapine in patients with bipolar disorder, mixed or depressed phase, and alcohol dependence. *Alcoholism: Clinical and Experimental Research*, *38*(7), 2113–2118.
- <sup>64</sup> Litten, R. Z., Fertig, J. B., Falk, D. E., Ryan, M. L., Mattson, M. E., Collin, J. F., et al. (2012). A double-blind, placebo-controlled trial to assess the efficacy of quetiapine fumarate XR in very heavy-drinking alcohol-dependent patients. *Alcoholism: Clinical and Experimental Research*, *36*(3), 406–416.

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- <sup>65</sup> Pettinati, H. M., O'Brien, C. P., & Dundon, W. D. (2013). Current status of co-occurring mood and substance use disorders: A new therapeutic target. *American Journal of Psychiatry*, 170(1), 23–30.
- <sup>66</sup> Ostacher, M. J. (2011). Bipolar and substance use disorder comorbidity: Diagnostic and treatment considerations. *FOCUS: The Journal of Lifelong Learning in Psychiatry*, 9(4), 428–434.
- <sup>67</sup> Farren, C. K., Hill, K. P., & Weiss, R. D. (2012). Bipolar disorder and alcohol use disorder: A review. *Current Psychiatry Reports*, 14, 659–666.
- <sup>68</sup> Farren, C. K., & McElroy, S. (2008). Treatment response of bipolar and unipolar alcoholics to an inpatient dual diagnosis program. *Journal of Affective Disorders*, 106, 265–272.
- <sup>69</sup> Weiss, R. D., Griffin, M. L., Jaffee, W. B., Bender, R. E., Graff, F. S., Gallop, R. J., & Fitzmaurice, G. M. (2009). A “community friendly” version of integrated group therapy for patients with bipolar disorder and substance dependence: A randomized controlled trial. *Drug and Alcohol Dependence*, 104(3), 212–219.
- <sup>70</sup> Swarbrick, M. (2006). A wellness approach. *Psychiatric Rehabilitation Journal*, 29(4), 311–314.
- <sup>71</sup> Substance Abuse and Mental Health Services Administration. (2016). *What individuals in recovery need to know about wellness*. (SMA) 16-4950. Rockville, MD: Substance Abuse and Mental Health Services Administration.
- <sup>72</sup> Substance Abuse and Mental Health Services Administration. (2012). *SAMHSA's Wellness Initiative: Information for consumers* [Brochure]. HHS Publication No. (SMA) 12-4567. Rockville, MD: Substance Abuse and Mental Health Services Administration.
- <sup>73</sup> Substance Abuse and Mental Health Services Administration. (2012). *SAMHSA's working definition of recovery* [Brochure]. Publication No. 12-RECDEF. Rockville, MD: Substance Abuse and Mental Health Services Administration.

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