End the
In the United States, bipolar disorder (BD) costs approximately $45.2 billion annually. People with this disorder use three to four times more healthcare resources, spend four times more on healthcare, and account for approximately 15% of psychiatric admissions and 5% of mental health visits. The average cost for treating a bipolar patient with one hospitalization is approximately $17,000.

The risk of suicide is 15 times higher among those with BD than in the general population. More than 90% of people with BD have recurrent illness with progressive functional deterioration. In addition, people with BD have a higher risk of cardiovascular disease, violence, and substance abuse. Untreated BD can reduce quality of life, social interactions, and daily function.

An adult with BD is either paralyzed by depression or energized by mania, with symptoms of distractibility, insomnia, grandiosity, flight of ideas, hyperactivity, and rapid speech and thoughts. Although medications and psychosocial treatments can improve quality of life, BD often remains untreated. Instead, bipolar signs and symptoms are misdiagnosed as depression.

This article focuses on adult BD and presents diagnostic considerations, as well as options for assessments, screening, and treatment.

Epidemiology of BD
BD is a chronic, unremitting, lifelong disorder that usually begins between the ages of 16 and 25. The rates of bipolar spectrum disorder in the general population range from 2.6% to 6.5%. Approximately 13% to 20% of people with BD are “rapid cyclers,” with more than four affective episodes a year.

Gender is not a significant risk factor. More than half the time, onset begins with a manic episode. With medication, a manic episode can last approximately 10 weeks, compared with 17 weeks without medication.

Genetic transmission and heritability play a major role, according to family, twin, and adoption research. Approximately 57% of monozygotic and 15% of dizygotic twins develop the disorder. Research to identify the specific genes, linkages, and associations that influence BD is ongoing.

Closer familial relationships increase the percentage of a genetic link to another person with BD. Pendulum reports the incidence of a genetic link to another person with BD is 1% for the general population. Incidence of BD for a person who has a family member with this disease is: 2nd degree relative 3%-7%, full brother/sister 15%-25%, a fraternal twin 15%-25%, 15%-30% for one parent and 50%-75% if both parents have BD. The genetic incidence is highest (70%) with an identical twin.

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Having a family member with depression increases a person’s risk of BD. Other factors can play a role in causing BD, such as environment and lifestyle choices (drug and alcohol use). No single causative factor of BD has been identified.

## Pathophysiology

Although patients seem to have alterations in circadian rhythm, the pathophysiology of bipolar mood swings is unknown. Some researchers have suggested anatomic changes in the amygdala and white matter, whereas others point to molecular changes in ATPase and signal transduction. Biologically, depression and mania have opposite neurotransmitter functions. Neurotransmitters (norepinephrine, serotonin, dopamine) regulate mood, movement, BP, and post synaptic impulse conduction, and also alter serotonin metabolism. They excite transmission. Gamma-aminobutyric acid (GABA) and other chemicals inhibit neurotransmission in the brain, and amines and receptor sensitivity to catecholamines regulate mood. Neurochemical theories of mania suggest an excess of catecholamines, such as norepinephrine, and norepinephrine is elevated in BD.

Other issues may include a serotonergic transmission deficit and GABA alterations. Researchers have studied abnormalities in the dopamine-rich areas of the brain. Psychosocial theorists believe the disorder responds to environmental stressors.

## Identifying BD in primary care

Approximately 80% of those who screen positive for BD are diagnosed incorrectly. Researchers report that 40% of bipolar patients were misdiagnosed with depression. Other misdiagnoses include schizophrenia, delirium, borderline personality disorder, multiple personality disorder, Axis II disorders, attention deficit hyperactivity disorder (ADHD), and substance abuse disorder. Additional medical issues may include anemia, fibromyalgia, and a low thyroid condition. It may take several years to establish an accurate BD diagnosis; bipolar I can take 6 years, and bipolar II can take up to 12 years.

Symptoms most frequently misdiagnosed include racing thoughts, excessive spending, distractibility, difficulty concentrating, euphoria, and excessive or risky behavior. Bipolar symptoms can be incorrectly attributed to a narcissistic, self-indulgent personality that engages in reckless promiscuity, drug abuse, or uncontrolled spending.

One study found that patients usually visit a range of providers, including psychiatrists (62%), primary care providers (54%), psychologists (47%), counselors or social workers (46%), and clergy (30%). The 20% of patients who received a correct diagnosis were identified primarily by psychiatrists (47.9%), psychologists or counselors (23.4%), and primary care providers (22.6%). Primary care providers need to expand their knowledge and skills to evaluate BD and enhance diagnostic accuracy.

## Bipolar spectrum disorder

The Diagnostic and Statistical Manual, Fourth Edition, Text Revision (DSM-IV TR) categorizes BD as an Axis mood spectrum disorder within a family of affective disorders. The classification is listed as three subtypes—BD I and II, and cyclothymia—or BD-NOS (not otherwise specified). (See BD and common comorbid conditions).

Non-BD I and II are sometimes referred to as BD III, IV, and V. In general, however, the diagnosis of BD-NOS is for patients who experience the same BD symptoms, but who do not meet the specific diagnostic criteria for BD II.

The subtypes of BD are challenging to differentiate, especially when presenting symptoms begin to approach the diagnostic criteria of depressive disorders. Making a correct diagnosis can be difficult, as other disorders may mimic BD. In addition, BD patients frequently present with a legitimate secondary diagnosis, such as illicit drug use or a personality disorder, which may be the causative problem.

To diagnose BD, clinicians must understand diagnostic definitions and their clinical presentation. The ability to look beyond the symptoms to the causative pathology is essential.

## Assessment

Accurate diagnosis requires a systematic and deliberate approach. The chief complaint may focus on symptoms of depression. A patient’s history may include mood swings and episodes of depression or euphoric behavior. Accounts of current or past symptoms of mania, hypomania, family history, age of onset, history, and premorbid functioning can provide data to improve diagnostic accuracy.

Signs of BD include previous failure to respond to antidepressants, an episode of mania during antidepressant treatment, significant alcohol use/abuse to self-medicate episodes of mania, and previous unipolar depression with mood swings. Developmental data may include behavior problems.
in school, which may be diagnosed as ADHD and suggest subsequent bipolar symptoms.

However, a history of behavior problems yields more information in patients born before 1990 rather than asking if a patient has had a specific diagnosis such as ADD/ADHD. If manic or “hyper” behavior occurred in childhood, a differential diagnosis of BD should be considered when formulating a plan of care. A neurobehavioral mental status exam can gather data regarding other psychiatric disorders and comorbidities. Family history may provide information about relatives with mood swings and disorders.

Differential diagnosis

BD should be differentiated from psychosis, including schizophrenia, borderline personality disorder, medical disorders, and ADHD. The hallmarks of BD include more mood symptoms (euphoria, elation, hyperactivity, agitation, depressive symptoms) than the thought patterns of hallucinations and delusions or negative symptoms (alogia, no motivation, flat affect) seen in schizophrenia.

The negative symptoms of schizophrenia may occur, but they are less common than mood disorders. People with BD have more comorbid disorders, such as substance abuse, anxiety, panic attacks, posttraumatic stress disorder, and cognitive impairment. (See Comparison of diagnostic categories and symptoms.)

BD patients are also more likely to have migraine headaches, obesity, and asthma. In addition, medical causes for mania need to be ruled out, such as infections, endocrine disorders, neurologic conditions, nutritional deficiencies, polycythemia, and systemic lupus erythematosus. Infections include AIDS, encephalitis, influenza, and tuberculosis. Endocrine disorders include Addison disease, Cushing disease, and hyper- or hypothyroidism. Possible neurologic disorders are central nervous system tumors, cerebrovascular events, delirium, epilepsy, and head trauma. Medications that may trigger manic states include amphetamines, anabolic steroids, anticholinergic agents, hallucinogens, levodopa, and opiates.

The longer it takes to make an accurate diagnosis, the greater the chance of psychosocial decline, costly hospitalizations, and suicide. If a patient is misdiagnosed with depression, antidepressants may precipitate a manic episode, a negative attitude toward treatment, and fear of medications.

Differential diagnosis

Diagnosis is also complicated because the American Psychiatric Association diagnostic criteria lack precision. People often under-report critical symptoms. In general, people with BD report more atypical and psychotic symptoms, mood lability, and psychomotor retardation than those with unipolar depression. They also tend to be more extroverted, novelty seeking, and less judgmental than those with unipolar depression. Patients with BD may also have other psychiatric disorders, so a comorbid disorder may be diagnosed instead of BD. Because these differences occur in symptoms and history, clinicians should improve diagnostic accuracy by examining longitudinal history and searching for a family history of BD, manic and hypomanic episodes, and mood

<table>
<thead>
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<th>BD and common comorbid conditions</th>
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<tr>
<td><strong>Comorbidities</strong></td>
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<tr>
<td>Alcohol abuse</td>
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<td>Substance abuse</td>
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<td>Obsessive compulsive disorder</td>
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<td>Panic disorder</td>
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<tr>
<td>Generalized anxiety</td>
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<td>Phobias</td>
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Data represented in percentages.

Differential diagnosis

Determining risky behaviors

A person with depression or BD should be screened for suicide risk and risk taking. The risk increases with a previous suicide attempt. Assessment includes physical risks, such as fast or reckless driving, high-risk sexual behaviors, and substance use or abuse. Safety is paramount and a plan must be established and implemented.

A physical exam is routinely normal for a person with BD, although the manic person may fidget and be distracted during an exam; a person who is depressed may have psychomotor slowing. A thorough cardiac exam with an ECG is useful before prescribing stimulant medications.

People with BD have an increased risk of suicide. Monitoring suicidal ideas, using medications that reduce impulsivity, and watching for exacerbation of BD symptoms can lower risk. Interventions that improve social interaction and set realistic goals can also help.

Depending on the severity and circumstances of suicide intent or threats, the plan of care may range from preventive teaching and counseling to initiating an involuntary hold for hospitalization. In order for an involuntary hold to occur, a person must be an immediate danger to himself or others or be gravely disabled. In addition, families should alert NPs to changes in behavior that require evaluation.

Determining lifestyle habits for caffeine intake, substance use, over-the-counter medications, exercise, smoking, and diet help identify areas that may interact with prescribed drugs. This information can lead to prescriptions for healthier behavior.
## Comparison of diagnostic categories and symptoms

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<thead>
<tr>
<th>Diagnosis</th>
<th>Diagnostic criteria/symptoms</th>
<th>Comments</th>
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| Major depression   | *Depressed mood or markedly diminished interest or pleasure in almost all activities*  
|                    | • Fatigue or loss of energy  
|                    | • Worthlessness  
|                    | • Impaired concentration, indecisiveness  
|                    | • Insomnia or hypersomnia  
|                    | • Psychomotor agitation or retardation  
|                    | • Recurring thoughts of death or suicide  
|                    | • Significant weight loss or gain (>5% of body weight/month)  
|                    | A constellation of the symptoms of depression that do not meet the criteria for major depression might qualify for atypical depression or seasonal affective disorder.                                                   | This is not a few days of the blues. People with fewer symptoms that endure may qualify for atypical or other categories of depression. |
| Depressive symptoms|                                                                                                                                   | Consider other depressive disorders including atypical depression or seasonal affective disorder. |
| Mania              | • Flying suddenly from one idea to the next  
|                    | • Rapid, “pressured” speech  
|                    | • Increased energy, with hyperactivity and decreased need for sleep; irritable  
|                    | • Grandiose and unrealistic perception of self and power  
|                    | • >3 symptoms present for at least 1 week  
|                    | May go on spending or gambling spree  
|                    | Cannot turn off their brain  
|                    | Needs little sleep  
|                    | Perception of reality is overcome by impulsivity and misperceptions. Will often not eat or sleep unless supervised in a quiet environment. Often self-medicates with drugs* |
| Hypomania          | • Flight of ideas from one to the next  
|                    | • Rapid, “pressured” speech  
|                    | • Increased energy, with hyperactivity and decreased need for sleep  
|                    | Shares characteristics of mania but rarely requires hospitalization. About 4% of population will experience hypomania. Patients feel happy and energized, and need little sleep. |
| Bipolar I          | At least one manic episode with depression or mixed (mania/depression right after the other)  
|                    | • Psychosis  
|                    | • Paranoia  
|                    | • Rapid mood cycling  
|                    | • Recurrent schizophrenia-like symptoms  
|                    | • Recurrent depression  
|                    | • Mania  
|                    | • Bizarre behavior  
|                    | • Substance abuse  
|                    | • Depressive episodes (see depression symptoms)  
|                    | Affects 1% of population. Must have at least 1 manic episode witnessed or verified.                                                                                                                                   | (continued)                                                                                     |
| Bipolar II         | *1 or more documented episodes of depression with one or more episodes of hypomania  
|                    | • Seasonal depression  
|                    | • Alcohol/substance abuse  
|                    | • Rapid mood cycling  
|                    | • Impulse difficulties  
|                    | • Recurrent depression  
|                    | • Mood instability  
|                    | If the patient has a diagnosis of mixed episodes or mania, he or she typically does not qualify for Bipolar II.                                                                                                           |
End the bipolar tug-of-war

Clinicians should also consider comments from family and friends regarding behaviors.

**Options for screening**

Screening can improve diagnosis by documenting symptoms, bipolar signs, and treatment response. A screening also evaluates the presence of anxiety, depression, BD, and other psychiatric problems.

Screening tools help identify symptoms of a mood disorder. Those who score above the cutoff for BD require a referral for evaluation and possible treatment. Screening can also identify substance abuse. If a patient depends on alcohol or psychoactive substances, detoxification may be warranted before BD symptoms can be evaluated.

Self-report tools are simple, short, and easy to complete, and they help measure changes in symptoms due to treatment. The Mood Disorder Questionnaire (MDQ), based on the DSM-IV-TR, has 15 yes-no questions and takes 5 minutes to score. A score over 7 suggests a bipolar spectrum disorder. The MDQ can identify 70% of people with this disorder while eliminating the diagnosis for 90% of people. In one study, concurrent validity was measured on a randomly selected group of 711 subjects obtained from a nationwide epidemiologic general population sample of adults.

To demonstrate concurrent validity, the subjects’ scores on the MDQ were compared with an abbreviated version of the Structured Clinical Interview for DSM-IV-TR. A sensitivity of 0.281 and specificity of 0.972 were obtained for the MDQ.

**Treatment considerations and challenges**

The diagnosis of BD is complicated, compliance with treatment is poor, and the suicide risk is high. A patient typically needs a provider who can move from outpatient to inpatient settings. The goal of treatment is to stabilize the patient, and NPs should collaborate with a psychiatrist on diagnosis and treatment.

Bipolar patients may require hospitalization, so they are best managed by a clinician with hospital privileges and treatment experience. Mood stabilizers are the primary pharmacologic intervention for both acute episodes and in prophylaxis. Based on consensus guidelines in the acute phase, the focus should be on ending the current manic, hypomanic, bipolar, or mixed episode. For prevention and maintenance, the focus is on long-term treatment to prevent recurrence. Treatment includes medications, psychotherapy, education, and support. Medication adverse reactions may include movement disorders and extrapyramidal effects.

For an acute bipolar depressive episode associated with BD 1, the medication is typically an olanzapine/fluoxetine combination (Symbyax). For acute mania, the medications include aripiprazole (Abilify), chlorpromazine (Thorazine), divalproex (Depakote), lamotrigine (Lamictal), lithium (Eskalith), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal), or ziprazidone (Geodon). For maintenance

### Comparison of diagnostic categories and symptoms (continued)

<table>
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<th>Diagnosis</th>
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<tbody>
<tr>
<td>Rapid cycling</td>
<td>A variation of BD. Mood state swings from manic or hypomanic to depressed and back again rapidly. Episodes of mania or depression may last days, weeks, or months. Ultradian cycle occurs hourly within a single day.</td>
<td>Affects 10%-24% of people with BD at some point during life. Management is challenging. DSM-IV-TR provides diagnostic algorithm to determine rapid cyclers. Rapid cyclers have increased comorbidities (for example, substance abuse), increased hospitalizations if misdiagnosed, and increased suicide attempt rates.</td>
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<tr>
<td>Cyclothymic disorder (BD-NOS or soft bipolar)</td>
<td>Relatively mild mood disorder with mood swing symptoms for &gt;2 years. Moods swing between short periods of mild depression and hypomania (elevated mood). The low and high mood swings never reach the severity of major depression or mania. Cyclothymia is a “bipolar-like” illness. Symptoms are milder than in full-blown BD.</td>
<td>About 50% will progress to BD I or BD II.</td>
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Evaluation of all disorders should include an assessment and monitoring of suicide risk.
The effectiveness of other drugs is unknown or they are unlikely to be beneficial. Relapse is prevented by lithium, although carbamazepine, cognitive therapy, education, family-focused psychoeducation, lamotrigine, valproate, or divalproex sodium can be beneficial.\textsuperscript{16,17}

Complete stabilization in every patient may not be possible. However, any reduction of the extreme highs and lows is therapeutic. An effective medication regime requires some trial-and-error and fine-tuning. Areas that impact the response include the actual medication class (mood stabilizer, antiepileptic drug, antidepressant, antipsychotic, antianxiety medications), specific medication within the class, dosage, and the combination of medications. It is unlikely that a single medication will be totally effective during all phases of illness. As many of these medications take several weeks to show therapeutic response, the process can be slow and frustrating for patients and providers. As such, other therapeutic interventions should be an essential part of any treatment plan.

Medication adverse reactions such as weight gain, diabetes, and a lipid level increase can complicate treatment compliance. Weight gain occurs most frequently with valproate, lithium, olanzapine, and clozapine. Drugs with lower risk of weight gain are ziprasidone, risperidone, and aripiprazole.

When weight gain is a possibility, a weight management program becomes a priority. Psychotropic medication-induced weight gain is often neglected because it is difficult to manage in clinical settings when the focus is on stabilization. An individual, comprehensive nutrition and exercise weight management program can be effective and should include educational modules on nutrition, wellness, healthy lifestyle, and fitness. Clinicians should also encourage a healthier

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**Case study**

**Present illness.** James was a charming and articulate 21-year-old African American college student. His friends brought him to the university health center because he was becoming more irritable and suspicious, and had a personality change. He believed he was depressed.

**Chief complaint.** He was sad, depressed, and unable to function for 3 months. He also stated he felt irritable, anxious, and unable to control angry impulses for 1 month.

**History.** He had done well in college until the previous semester, but now felt isolated and alienated. After stating that he had not slept for 4 nights and was going to invent a new vaccine to save the planet, he was referred to urgent care at the local hospital. He initially denied any prior illness. He reported that some family members had a history of depression or had “nerve” problems. He said it was difficult to go to school and church, but he just goes through the motions. He was not sure life was worth living. He reported always being “on the go” and hyper. He denied prior depression but had mood swings every couple of years.

**Psychosocial issues.** He drank two to four cups of caffeine a day and two cans of soda. James lived at home with a supportive family. He smoked, rarely exercised, liked junk food, and had a basal metabolic index of 22. He also drank beer and wine. He occasionally smoked marijuana. He denied any other drug use.

**Suicide risk assessment.** He had thought about suicide but had no current plan, method, or means. He denied prior suicide attempts.

**Prior medical history.** He had occasional hay fever and treated it with over-the-counter medications.

**Physical exam.** His exam and vital signs were within normal limits.

**Appearance.** A disheveled, unwashed 21-year-old James was constantly fidgety and paced around the interview room admiring the art. He picked up and played with everything he saw.

**Screening.** James scored a 12 on the MDQ. This score suggests BD and a need for a more thorough psychiatric evaluation.

**Psychiatric consult.** A psychiatrist concurred with the diagnosis of moderate BD without rapid cycling.

**Prescription:** Divalproex with subsequent potential addition of an antidepressant or lithium.

**Course of treatment.** James was diagnosed with depression when he was a teenager, but said it was not accurate. He did not think anything is wrong or that he needed his medications, but agreed to try them for a while. When he felt depressed, he did not want to live, so he was willing to try medications and psychotherapy.

**Plan and patient education.** BD and the usual effects of drugs and possible adverse reactions were discussed. James received a fact sheet on medications and BD. He scheduled an appointment in 2 weeks for follow-up to discuss the effects of the medication. James was informed of resources and support groups, and encouraged to read about BD. He was asked to complete a log documenting daily moods.

**Outcomes.** With therapy and mood stabilizers, James’ symptoms decreased. With a course of mood stabilizers, education, and cognitive therapy, his sense of humor and energy returned. He also went back to school. His suicide risk was monitored, and it decreased over time. He participated in activities he enjoyed, started working at a video store, joined a BD support group, and maintained close contact with his family. His MDQ score decreased from 12 to 9.
lifestyle with weight management, healthy eating, portion control, and exercise.

The NP may provide counseling and support, and negotiate individualized goals or recommend weight management programs. A program should emphasize increased exercise, such as walking and diet modifications, such as avoiding foods high in fat. Early intervention is the key to prevention.11

Medications may exacerbate other comorbid disorders, so BD medications with the least likelihood of destabilizing mood should be selected.2 Avoid addictive medications such as benzodiazepines if a substance abuse disorder exists.

In the systematic treatment enhancement program for BD, 4,360 patients were followed long term to evaluate treatment effectiveness.20 Slightly more than half (58%) of 1,469 patients with 2 years of participation in this project recovered and had only two symptoms of the disorder during an 8-week period at the 2-year follow-up. The recovery group was likely to be white and female, with better finances, education, and health insurance. They had a lower level of depression and symptoms at the onset and typically did not live alone. Almost half of those who recovered also had a recurrence during the 2-year follow-up and most people (70%) returned to the depression. Residual symptoms (depression or mania) and a coexisting psychiatric illness predicted recurrence.23 However, limited information about psychosocial interventions existed.

Daily dosing, using medication containers, and family monitoring can improve medication adherence. Frequently monitoring blood levels can also improve adherence. The patients who have better adherence participate in treatment selection, self-monitor mood and symptoms, recognize early signs of a relapse, participate in bipolar support alliance, and learn about BD.

**Employing psychotherapy**

Therapeutic approaches, including cognitive behavioral, social rhythm, and interpersonal therapies, can enhance recovery and relieve symptoms. If the patient has a strong support system, family therapy is also beneficial because they can recognize the triggers of the cycling.21

Cognitive therapy can reduce distorted thinking involved with beliefs. It can reduce medication noncompliance and the frequency of hospitalization. In addition, it can teach patients to monitor prodromal symptoms and seek medication adjustment when symptoms recur or increase. Self-help mood disorder manuals, self-help groups, and the bipolar support alliance also encourage wellness and coping.

Social rhythm therapy or light and dark therapy may be helpful. Patients have reported benefits from meditation, yoga, and acupuncture.

Medication adherence is essential, and clinicians should identify barriers to adherence and their subsequent solutions. Lapses in medication adherence can result in severe or even life-threatening outcomes. Extreme treatment—out of the NP’s scope of practice—is ECT,22 which is used in treatment-resistant cases.

Education helps people understand the triggers of the illness and behaviors that antagonize the disease process, such as substance abuse or a poor sleep schedule. Explaining the nature, myth, and treatment of BD helps patients take an active role in making decisions and managing self-care.

Patients and families need to understand BD is not caused by a weak will. Instead, it is a biological disorder that responds to medications and therapy. Families can learn to observe and report medication effects, encourage social contacts, and support self-esteem. Family members can report signs of relapse or impending mania, such as reckless behavior, irritability, anger, unusual sexual ideas, poor judgment, impulsivity, spending sprees, or legal infractions.

Signs of impending depression include sadness, anhedonia, slowed behavior, and somatic symptoms (weight loss, insomnia, constipation). Therapy or support groups also help teach coping strategies. The NP should understand that close family and friends may be frustrated and angry at the patient, who they blame for bringing financial chaos and emotional turbulence into their lives. It will be a long-healing process for all involved.

Although the relationship between stress and BD is not well understood, people with BD typically have more severe stressors before episodes. Stress and negative life events influence relapse and recovery time. One theory is that stress disrupts the normal circadian rhythms, sleep cycles, and physiologic patterns. Interventions can focus on the family to reduce conflict and implement interpersonal therapy to improve negotiating dilemmas, role transitions, and stable routines.

With proper diagnosis and treatment, patients with BD can function well at school, work, and home, and are usually asymptomatic between episodes. Many patients with a consistent, predictable cycling pattern can maintain a high level of function by scheduling time off to work around a bipolar cycle.

Clinicians who know the screening tools, assessment, treatment challenges, and appropriate interventions can increase the quality of their life for people with BD. Updating knowledge of BD can lead to more timely diagnosis and treatment. As a result, this can increase psychosocial functioning and create better medication compliance, and aid the prevention of many suicides. NPs must realize their vital role in the treatment of this debilitating mental illness. ☞
REFERENCES

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