MEDIPULSE BRIEF

What is Bipolar Disorder?

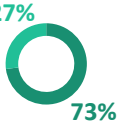
Bipolar Disorder (BPD) is a chronic mood disorder characterized by episodes of mania/hypomania and depression, with or without mixed features.[1-3] Bipolar I is a subtype of bipolar disorder. To be diagnosed as Bipolar I disorder (BP-I), patients are required to have at least one manic episode and can also experience depressive or hypomanic episodes. Patients with bipolar disorder are **17 times more likely to die by suicide** than the general population. In fact, 26% of patients with bipolar disorder attempt suicide at least once in their life.[4-5] Based on data from the National Comorbidity Survey in 2007, the estimated lifetime prevalence of bipolar disorder for adults in the US is 4.4%. The average onset of Bipolar I disorder is 20 years of age. About 30-60% of patients with bipolar disorder have difficulties in performing daily life routines.[6-9]

Employer Impact

Bipolar disorder peaks at the most productive working years of **25-39** years of age. It is a leading cause of disability[4], has a high rate of recurrence[5], increases the risk of suicide[5], and can cause cognitive impairment.[11]

50% Approximately **50%** of patients with BPD work below their qualifications, part-time, in a limited capacity or are unable to work.[12]

Bipolar I disorder patients incur approximately $119.8 billion more in annual societal costs than the general population, or $48,333 per patient. **73%** ($87.8 billion) and **27%** ($32 billion) of this amount are driven by indirect and direct costs, respectively.[13]



Many patients refuse or are unable to see a mental health specialist due to factors such as: disease stigma, insurance coverage, and financial burden. The wait time between specialist referral and office visit is often 6 weeks to 6 months. To complicate these delays, the predominance of depressive symptoms often lead to misdiagnosis as Major Depressive Disorder (MDD).[14] Delays in diagnosis have been associated with more frequent mood episodes, increased suicidal behavior, employment challenges, financial difficulties, and relationship issues.[15-17]

Data collected in 2019 from two commercially insured cohorts showed that patients initially diagnosed with MDD who received a subsequent bipolar I diagnosis had significantly higher all-cause medical costs compared to patients initially diagnosed with bipolar I disorder (cost difference of $8,250). The same pattern was observed for mental health-related costs, with a cost difference of $7,425).[18]

Work performance was assessed in the World Health Organization's (WHO) Health and Work Performance Questionnaire (HPQ) using self-reported absenteeism (missed days of work) and presenteeism (low performance while at work transformed to lost workday equivalents) generating a summary measure of overall lost workdays.[19]

BPD costs employers approximately 96.2 million lost workdays and $14.1 billion per year in lost productivity

BPD with major depressive episodes was consistently associated with significantly more lost work performance than MDD

Clinical Features of BP-I[1]

Manic Features

Depressive Features

Bipolar I Disorder*

- Grandiosity
- Persistently increased energy
- Abnormal mood
- Irritability
- Decreased need for sleep
- Pressured speech
- Racing thoughts
- Distractibility
- Impulsivity
- Increased sexual drive
- Recklessness
- Social intrusiveness

- Depressed mood
- Loss of interest or pleasure
- Significant weight change
- Insomnia or hypersomnia
- Psychomotor agitation
- Loss of energy
- Feeling of worthlessness
- Indecisiveness
- Recurrent thoughts of death

*For diagnosis of bipolar I disorder, it is necessary to meet the criteria for a manic episode.

Bipolar Disorder is thought to result from an imbalance in the monoamine neurotransmitter systems with both genetic and environmental factors contributing to disease development. The exact cause of bipolar disorder is currently unknown. Gene- Environment interactions can lead to neuronal changes that affect the body in a variety of ways resulting in cognitive and psychosocial impairment.[10]

Diagnosis

Patients with bipolar disorder may experience delays in diagnosis and treatment and are often misdiagnosed. Women are more likely than men to be misdiagnosed with depression (68% vs 43%) while men are more likely than women to be misdiagnosed with schizophrenia (28% vs 14%).

BPD is commonly misdiagnosed as MDD, as patients tend to seek care during a depressive episode. The average delay from patient reported symptom onset to treatment is approximately 10 years. In order to be diagnosed with BP-I, it is necessary to meet the criteria for a manic episode; however, a manic episode may be preceded by and may be followed by hypo-manic or major depressive episodes. [1-3]

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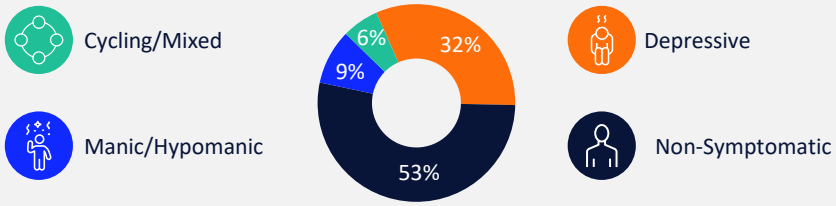
SYMPTOMS

The symptoms of a depressive episode are identical in bipolar I disorder (BP-I) and major depressive disorder (MDD).[1] Mild mania may be easy to miss during an office visit and symptoms are variable from patient to patient.[20] Symptoms can be masked if the patient also suffers from anxiety, panic disorder, or substance abuse. Depressive symptoms are the most common symptoms in bipolar disorder and patients generally experience multiple depressive episodes.[21]

Bipolar I Disorder Symptoms During Course of Illness (% Weeks With Symptom Type)[22]



Based on a longitudinal, prospective study of 146 patients with bipolar I disorder who were followed for a mean of 12.8 years

Treatment options

Several antipsychotics and mood stabilizers have been approved by the FDA for the treatment of bipolar I disorder. Although patients with bipolar I disorder spend more time in depression than in mania or hypomania, few studies focus on depressive episodes.[10] Four medications have been approved by the FDA for bipolar I depression, all of which are antipsychotics.[23] There are two medications approved by the FDA to treat adults with depressive, acute manic and mixed episodes associated with bipolar I disorder. Lifestyle modifications and various forms of psychotherapy have been proven to be beneficial for many patients as well.

Medications[10]

- Antipsychotics
- Mood stabilizers

Therapy[24]

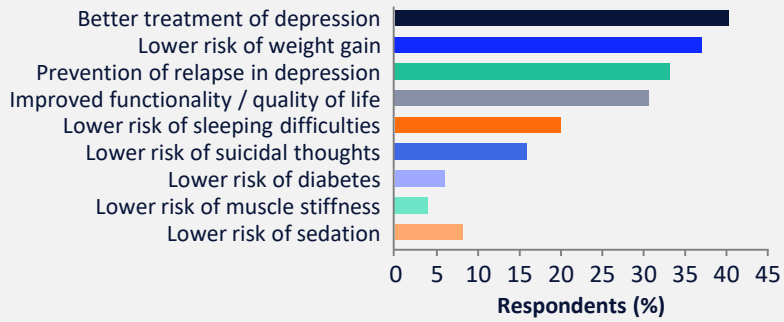
- Cognitive behavioral therapy
- Family-focused therapy
- Interpersonal therapy
- Social rhythm therapy
- Group psychoeducation

Lifestyle Interventions[25]

- Nutrition
- Exercise
- Coping strategies
- Attitudes towards health

Patient Identified Unmet Needs in Bipolar Disorder[26]

Aspects of Care that Patients Want Improved



Understanding patients' Needs, Interactions, Treatment, and Expectations (UNITE) global online survey of 1,300 patients with bipolar disorder.

Unmet need

Despite the availability of prescription and non-prescription treatments, there are still unmet needs in the treatment of bipolar disorder. Patients and providers have identified a need for better treatment of depressive episodes and more tolerable adverse event profiles for medications. Given these unmet needs and the variable efficacy and tolerability of current treatment options, it is important that patients and providers have a wide variety of treatment options available to enable individualized care plans for patients.

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