Bipolar Disorder: Diagnosis, Pathophysiology, and Management

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Definition

Bipolar disorder is a **chronic mood disorder** characterized by **pathologic fluctuations between mania/hypomania and depression**.

It is classified as a **mood disorder** in DSM-5-TR.

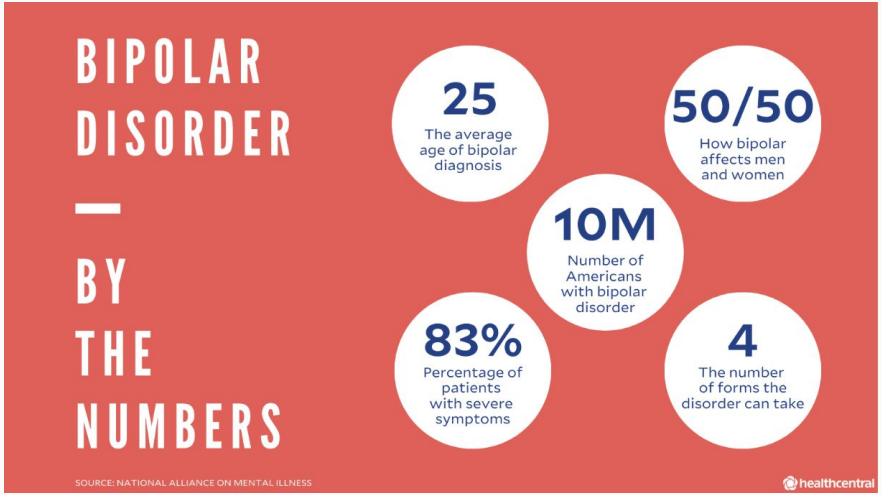
Core features include:

- Episodes of **mania or hypomania**
- Episodes of **major depression**
- Periods of **euthymia between episodes**

The illness significantly impacts:

- cognition
- behavior
- sleep
- energy
- judgment
- psychosocial functioning

Epidemiology



Lifetime prevalence:

- Bipolar I disorder: **~1%**
- Bipolar II disorder: **~1–2%**
- Bipolar spectrum disorders: **up to 4–5%**

Age of onset:

- Typically **late adolescence to early adulthood (18–25 years)**

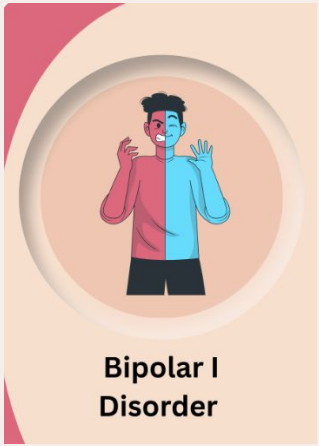
Gender distribution:

- Bipolar I: **equal in men and women**
- Bipolar II: **more common in women**

Other epidemiologic features:

- High heritability (~70–80%)
- Strong association with **substance use disorders**
- Elevated risk of **suicide (15–20%)**

Bipolar Spectrum Disorders

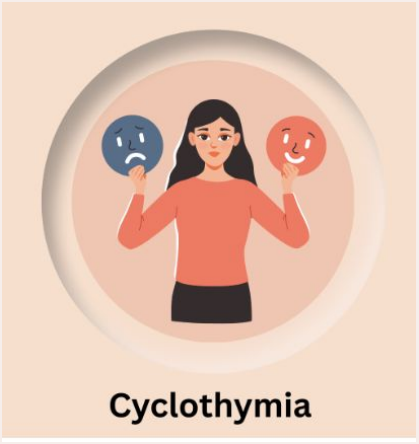


Bipolar I Disorder

- At least **one manic episode**
- Major depressive episodes common but not required

Bipolar II Disorder

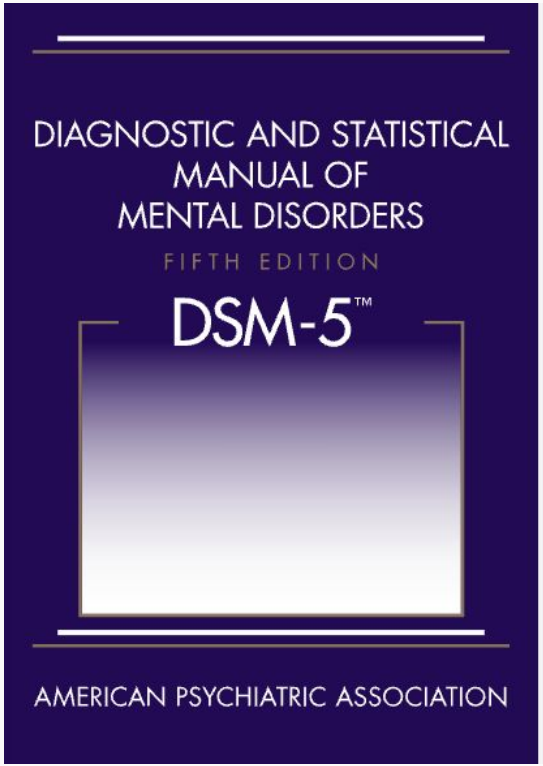
- **Hypomanic episode + major depressive episode**
- No history of mania



Cyclothymic Disorder

- ≥2 years of fluctuating **subthreshold hypomanic and depressive symptoms**

Diagnostic Criteria



DSM-5 criteria require:

A **distinct period of abnormally elevated, expansive, or irritable mood AND increased energy/activity**

Duration:

≥ 1 week (or any duration if hospitalization required)

PLUS **3 or more symptoms** (4 if mood is only irritable):

Mnemonic: **DIG FAST**

- **D**istractibility
- **I**ndiscretion / impulsivity
- **G**randiosity
- **F**light of ideas
- **A**ctivity increase
- **S**leep decreased
- **T**alkative / pressured speech

Symptoms must cause:

- marked impairment
- hospitalization
- psychosis

Hypomania and MDD in Bipolar Disorder

Hypomania

Hypomania shares similar symptoms with mania but differs in severity.

Key differences:

Duration:

≥ 4 days

Severity:

- **No marked impairment**
- **No hospitalization**
- **No psychotic features**

Patients often experience:

- increased productivity
- elevated mood
- decreased need for sleep

Hypomania is characteristic of **Bipolar II disorder**.

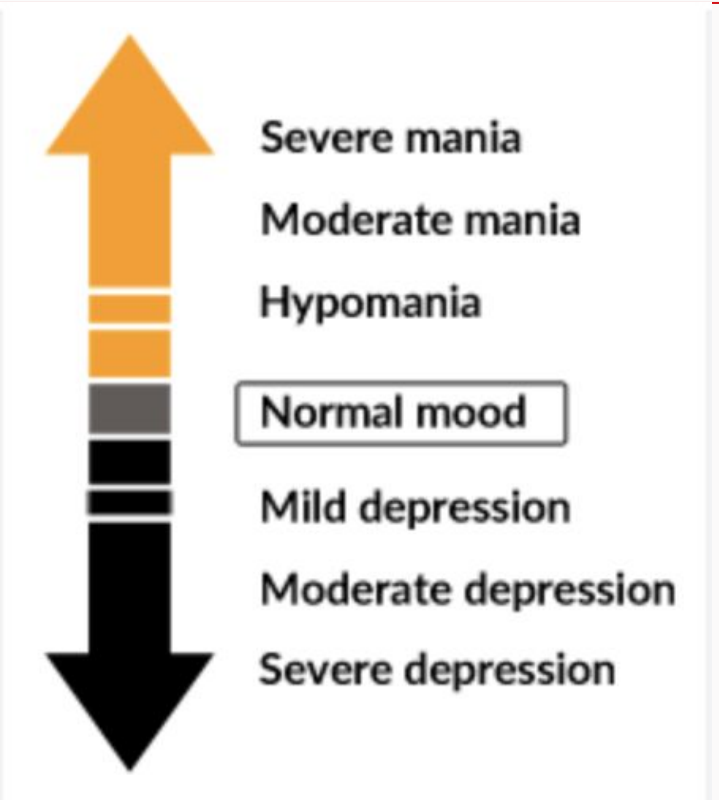
MDD in Bipolar Disorder

Criteria are identical to **Major Depressive Disorder**.

Symptoms for **≥2 weeks** include:

- depressed mood
- anhedonia
- fatigue
- sleep disturbance
- appetite changes
- psychomotor agitation or retardation
- impaired concentration
- feelings of guilt or worthlessness
- suicidal ideation

Diagnosis requires **≥5 symptoms including depressed mood or anhedonia**.



Clinical presentation , Pathophysiology & Genetic Factors

Clinical Presentation

Manic patients may present with:

• decreased need for sleep
• pressured speech
• grandiose ideas
• impulsive behaviors (spending, sex, travel)
• irritability
• agitation

Severe mania may involve:

• **psychosis**
• **delusions of grandeur**
• **disorganized behavior**

Depressive episodes often include:

• severe fatigue
• cognitive slowing
• hopelessness
• suicidal ideation

Pathophysiology

The exact mechanism remains multifactorial.

Key theories include:

Neurotransmitter Dysregulation

• Dopamine ↑ during mania
• Serotonin ↓ during depression
• Norepinephrine instability

Neuroanatomical Changes:
Neuroimaging studies show abnormalities in:

• prefrontal cortex
• amygdala
• hippocampus
• anterior cingulate cortex

Circadian Rhythm Disruption:
Abnormalities in biological clock genes influence mood cycling.

Genetic Factors

Bipolar disorder is among the **most heritable psychiatric disorders**.

Twin studies:

• Monozygotic concordance: **~60–80%**
• Dizygotic concordance: **~20%**

Genome-wide association studies (GWAS) implicate genes involving:

• calcium signaling pathways
• synaptic regulation
• neuronal excitability

Examples:

CACNA1C gene
ANK3 gene

Differential Diagnosis

Important conditions to consider:

Major Depressive Disorder

ADHD

Schizoaffective Disorder

Borderline Personality Disorder

Substance-induced mood disorder

Medical causes:

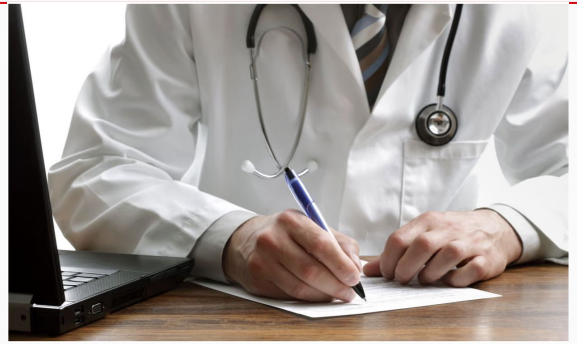
- hyperthyroidism
- Cushing syndrome
- neurologic disorders

Medical Evaluations

Before diagnosing bipolar disorder, clinicians should rule out medical causes.

Recommended workup may include:

- Thyroid function tests
- CBC
- CMP
- Urine toxicology
- Vitamin B12 / folate
- Neuroimaging if neurological symptoms present



Treatment overview

Mood Stabilizers

Lithium

Mechanism:

• modulates second messenger systems
• influences neurotransmitter release

Clinical benefits:

• anti-manic
• anti-depressive
• **reduces suicide risk**

Monitoring:

• serum lithium levels
• thyroid function
• renal function

Anticonvulsant Mood Stabilizers

Common agents include:

Valproate

• highly effective for acute mania

Lamotrigine

• effective for **bipolar depression and maintenance**

Carbamazepine

• alternative for refractory mania

Side effects vary but may include:

• hepatotoxicity
• rash
• hematologic abnormalities

Atypical Antipsychotics

Second-generation antipsychotics are frequently used.

Examples:

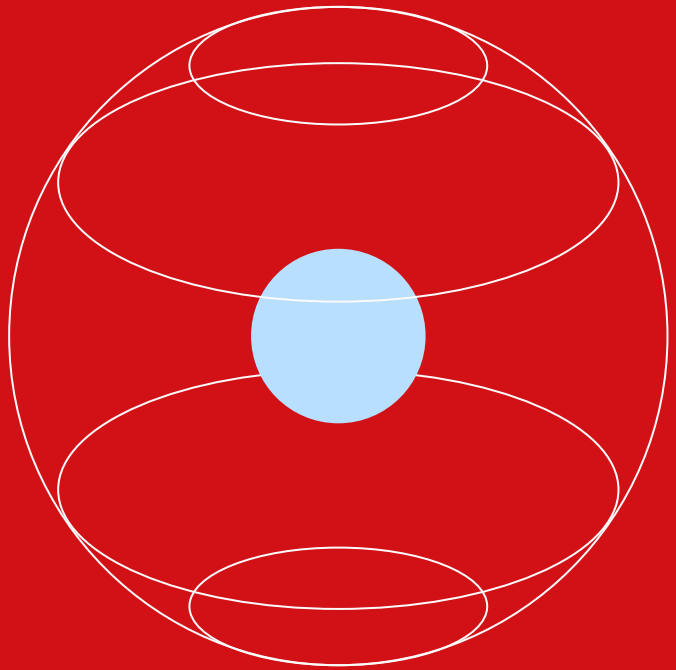
• Quetiapine
• Olanzapine
• Risperidone
• Aripiprazole
• Lurasidone

Indications:

• acute mania
• bipolar depression
• maintenance therapy

Mechanism involves **dopamine and serotonin receptor modulation**.

Treatment continued



Psychotherapy

Psychotherapy improves adherence and reduces relapse.

Evidence-based therapies include:

Cognitive Behavioral Therapy (CBT)

Interpersonal and Social Rhythm Therapy

Family-Focused Therapy

Psychoeducation is critical to help patients:

- recognize relapse warning signs
- maintain sleep routines
- adhere to medications

Prognosis & Suicide Risk

Prognosis

Bipolar disorder is **chronic but manageable**.

Important prognostic factors:

Better outcomes:

- early treatment
- strong social support
- medication adherence

Poorer outcomes:

- substance abuse
- rapid cycling
- delayed diagnosis

Patients experience an average of **9–10 episodes over a lifetime**.

Suicide Risk

Suicide risk is significantly elevated.

Statistics:

- ~25–50% attempt suicide
- ~15% die by suicide

Highest risk occurs during:

- depressive episodes
- mixed states
- early illness course

Lithium has been shown to **reduce suicide risk**.

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