BIPOLAR AND RELATED DISORDERS

Bipolar I Disorder

BD-I

DSM-5-TR 296.4X-296.7X | ICD-10-CM F31.X

A lifelong episodic illness defined by at least one manic episode, with depression carrying most of the symptomatic burden.

LIFETIME PREVALENCE	TYPICAL ONSET	SEX RATIO	COURSE
~1% (US adults)	Age 18-22; median ~20	~1:1 female:male	Recurrent; ~90% relapse

CLINICAL PICTURE

- Mania presents with elevated or irritable mood, decreased need for sleep, pressured speech, and goal-directed overactivity lasting a week or more.
- Insight collapses during mania; patients experience grandiose plans as genuine capability and resist treatment as unwanted interference.
- Psychosis occurs in more than half of manic episodes and is typically grandiose or persecutory and mood-congruent in content.
- Depressive episodes outnumber manic ones roughly three to one over time and account for most disability and most suicide risk.
- Mixed features, meaning agitated depression with racing thoughts, are common and carry elevated suicide and switching risk.
- Between episodes many patients retain subsyndromal symptoms and measurable deficits in attention, memory, and executive function.

DIAGNOSTIC CRITERIA AT A GLANCE

- Requires at least one manic episode: abnormally elevated, expansive, or irritable mood with increased activity for a week or any hospitalization.
- Three additional symptoms are required, or four if mood is only irritable, spanning grandiosity, reduced sleep need, pressured speech, and risky behavior.
- Mania must cause marked impairment, require hospitalization, or include psychotic features; hypomania by definition does none of these.
- Depressive and hypomanic episodes are extremely common but are not required for the diagnosis once a manic episode has occurred.
- Specify current episode type, severity, psychotic features, and course specifiers including rapid cycling of four or more episodes yearly.

NEUROBIOLOGY & PHYSIOLOGY

- Heritability is roughly 60 to 85 percent, among the highest in psychiatry, with substantial polygenic overlap with schizophrenia and depression.
- Dopaminergic hyperactivity underlies mania while subsequent receptor downregulation may drive the depressive switch in the dysregulation model.
- Amygdala hyperreactivity with reduced ventral prefrontal modulation impairs emotional regulation across manic, depressed, and euthymic states.
- Mitochondrial dysfunction, abnormal intracellular calcium signaling, and altered GSK-3 activity are among lithium's putative molecular targets.
- Circadian and social rhythm instability is central; sleep loss reliably precipitates mania and functions as both a symptom and a trigger.
- White matter hyperintensities, progressive cognitive decline, and elevated cardiovascular mortality shorten lifespan by roughly 10 to 20 years.

PSYCHOLOGICAL MECHANISMS

- Behavioral activation system dysregulation predicts manic response to goal attainment and to reward-relevant life events.
- Social zeitgeber theory holds that disrupted daily routines and sleep-wake schedules destabilize circadian rhythms and precipitate episodes.
- Hyperpositive self-appraisal and denial of illness drive medication discontinuation, which remains the leading proximate cause of relapse.
- Prodrome recognition, personalized early warning signs, and a rehearsed rapid action plan form the core psychoeducational target.
- High expressed emotion in families, particularly criticism and overinvolvement, predicts shorter time to relapse and worse functional outcome.

DIFFERENTIAL & COMORBIDITY

- Distinguish from schizoaffective disorder by whether psychosis persists two or more weeks in the absence of prominent mood symptoms.
- Rule out substance-induced mania, corticosteroid effects, hyperthyroidism, and antidepressant-induced switching before making the diagnosis.
- Borderline personality disorder shows mood shifts lasting hours, reactive to interpersonal triggers, without sustained reduction in sleep need.
- Substance use disorders co-occur in roughly 40 to 60 percent of patients, alongside anxiety disorders, ADHD, and metabolic syndrome.
- Lifetime suicide attempt rates approach 30 percent and mortality is many times the general population, peaking in mixed and depressive states.

Treatment EVIDENCE-BASED MANAGEMENT

PHARMACOLOGIC

- **Lithium 0.6-1.2 mEq/L** remains first line and uniquely reduces suicide; monitor levels, renal function, thyroid, and serum calcium.
- **Valproate 50-125 mcg/mL** is useful for mixed states and rapid cycling but is teratogenic and contraindicated in pregnancy.
- Second-generation antipsychotics including **quetiapine 400-800 mg/day**, olanzapine, and aripiprazole treat acute mania within several days.
- For bipolar depression use **quetiapine**, **lurasidone 20-120 mg/day**, or olanzapine-fluoxetine rather than antidepressant monotherapy.
- **Lamotrigine 100-200 mg/day** prevents depressive relapse; titrate slowly across 6 weeks to reduce the risk of serious rash.

PSYCHOTHERAPY

- Illness-focused **psychoeducation** across roughly 6 to 21 sessions reliably reduces relapse and improves medication adherence.
- **IPSRT** stabilizes sleep-wake and social routines and lengthens time to recurrence, particularly for depressive episodes.
- **Family-focused therapy** across about 21 sessions reduces relapse by lowering expressed emotion and improving communication skills.
- **CBT** targets residual depression and dysfunctional attitudes, with the largest effects seen early in the illness course.
- Psychotherapy is always adjunctive here; no evidence supports psychotherapy alone for the treatment of acute mania.

ADJUNCT & SUPPORTIVE

- **ECT** is highly effective for refractory mania, mixed states, catatonia, and severe bipolar depression including during pregnancy.
- Enforce sleep regularity, avoid shift work and rapid time-zone travel, and treat comorbid substance use aggressively and early.
- Track with the **YMRS**, **MADRS**, and a daily mood chart; patient-kept charts often reveal seasonal and cyclic patterns.
- Baseline and periodic metabolic screening, ECG where indicated, and explicit pregnancy planning discussions are standard of care.
- Escalate to inpatient care for mania with psychosis, judgment impairment endangering finances or safety, or acute suicidality.

CLINICAL PEARLS

- One manic episode makes it Bipolar I forever, regardless of later depressions.
- Lithium is the only agent with consistent anti-suicide evidence.
- Sleep loss is both prodrome and cause of mania; protect it first.

References

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NOTE

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