THE BIPOLAR SPECTRUM

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Criteria</th>
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<tbody>
<tr>
<td>Bipolar I disorder</td>
<td>Diagnosis can be made after one (1) manic episode</td>
</tr>
<tr>
<td>(mixed mania)</td>
<td>A hypomanic or depressive episode may occur before or after the manic episode</td>
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<tr>
<td></td>
<td>Not explained by a diagnosis categorized as a schizophrenia spectrum disorder</td>
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<tr>
<td>Bipolar II disorder</td>
<td>One hypomanic episode and at least one major depressive episode</td>
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<tr>
<td>(mixed hypomania)</td>
<td>No history of a manic episode</td>
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<td></td>
<td>Depressive symptoms or frequent alteration between depression and hypomania result in clinically significant distress or impairments of functioning</td>
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<tr>
<td>MDD with mixed features</td>
<td>Period of abnormally and continually elevated, expansive, or irritable mood with increased activity or energy for at least 4 consecutive days</td>
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<tr>
<td>(subsyndromal hypomania)</td>
<td>Impairment in social or occupational functioning is not severe</td>
</tr>
<tr>
<td>MDD</td>
<td>Hospitalization is not required, and there are no psychotic symptoms</td>
</tr>
<tr>
<td>(non-mixed)</td>
<td>Episode not attributable to a drug of abuse, a med, or other text</td>
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MANIA VS. HYPOMANIA:

<table>
<thead>
<tr>
<th>Mania</th>
<th>Hypomania</th>
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<tbody>
<tr>
<td>* Time period of at least 1 week* of abnormal mood that is elevated, expansive or irritable</td>
<td>* Period of abnormally and continually elevated, expansive, or irritable mood with increased activity or energy for at least 4 consecutive days</td>
</tr>
<tr>
<td>* = any time period if hospitalization is required</td>
<td>* Impairment in social or occupational functioning is not severe</td>
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<tr>
<td>Significant increase in goal-directed activity or energy</td>
<td>Hospitalization is not required, and there are no psychotic symptoms</td>
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<tr>
<td>The disturbance causes significant social/occupational functioning</td>
<td>Episode not attributable to a drug of abuse, a med, or other text</td>
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<tr>
<td>Hospitalization is required or psychotic features are present</td>
<td>EXCEPTION: antidepressants can precipitate an episode</td>
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<tr>
<td>Episode is not the result of a substance (drugs of abuse, meds, treatment, medical condition)</td>
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<tr>
<td>o EXCEPTION: antidepressants can cause a polarity switch</td>
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</tbody>
</table>

3 of the following (or 4, if mood is only characterized as expansive or elevated])

- Inflated self-esteem of grandiosity
- Decreased need for sleep
- Increased quantity of speech, or speech that is pressured
- Engaging in activities that can result in detrimental outcomes

- Flight of ideas or subjective racing thoughts
- Easily distracted
- Increased goal directed activity or psychomotor agitation

MAJOR DEPRESSIVE EPISODE:

- The criteria for a major depressive episode associated with bipolar disorder are the same used to diagnose a MDD with major depressive disorder

BIPOLAR DISORDER SUBTYPES

BIPOlar I DISORDER:
- Diagnosis can be made after one (1) manic episode
- A hypomanic or depressive episode may occur before or after the manic episode
- Not explained by a diagnosis categorized as a schizophrenia spectrum disorder

BIPOlar II DISORDER:
- One hypomanic episode and at least one major depressive episode
- No history of a manic episode
- Depressive symptoms or frequent alteration between depression and hypomania result in clinically significant distress or impairments of functioning

CYCLOTHYMIC DISORDER:
- Uncommon
- For at least 2 years, there are significant periods of hypomanic and depressive symptoms that never met full criteria
- Significant distressed or impaired functioning
- During this time period, at least 50% of time is spent with hypomanic or depressive symptoms

SPECIFIERS FOR BIPOLAR AND RELATED DISORDERS:

- Specifiers are included with a diagnosis to provide additional information regarding a specific patient
- Can guide pharmacologic decision making
- More than 1 specifier may be given

ANXIOUS DISTRESS:
- At least 2 anxiety sx present during current or most recent episode
- May further specify the severity based on number of symptoms
- Feeling keyed up/tense, unusually restless, difficulty concentrating because of worry/fear of losing control

RAPID CYCLING:
- At least 4 separate mood episodes (mania, hypomania or depressive) have occurred in the previous 12 months
- Episodes are separated by partial or full remission, or there is a switch to the opposite polarity that is not caused by a substance or another medical condition (EXCEPTION: ANTIDEPRESSANTS)

IMPACT OF RAPID CYCLING:
- More likely to have an earlier lifetime onset of symptoms
- Cycling often begins with depressive sx and can result from antidepressant use
- Women more likely than men
- Rapid cyclers are at increased risk for suicide attempts

IMPACT OF MIXED FEATURES:
- A manic episode with mixed features = greater irritability and more severe mood lability compared with non-mixed
- Dysphoric mood, excessive guilt, and suicidality = predominate depressive symptoms
- Increased number of lifetime episodes, increased risk of suicidality, longer time to episode resolution

OTHER SPECIFIERS:
- Melancholic features
- Atypical features
- Psychotic features
- With catatonia
- With peripartum onset
- With seasonal pattern

GOALS OF THERAPY:
- Remission (of current mood episode)
- Maintenance of response
- Prevention of relapse
- Full functional recovery (most challenging)

TREATMENT PHARMACOLOGY:
- BZDs and Mood Stabilizers modulate GABA & glutamate
- Clozapine, quetiapine, olanzapine and VPA are suggested activate DNA-demethylation of GABAergic gene promoters to correct downregulation
**TREATMENT SCENARIOS – ACUTE:**

### MANIC EPISODE:
- Reduce agitation, aggression, and impulsivity to prevent harm to self or others
- First line options = **lithium, valproate, or SGA**
  - Lithium for purely euphoric mania episodes
  - SGA better if aggression is present
- Combination of lithium or VPA with an SGA may be more effective than these agents alone (esp. with psychotic features)
- BZDs have anti-manic properties; can be used as short-term adjunctive treatment for psychomotor agitation, anxious features or sleep restoration
- Antidepressants should be tapered and discontinued when possible

### MANIC EPISODES WITH MIXED FEATURES:
- Consideration of VPA, carbamazepine or SGA
  - SGA as monotherapy or in combo with mood stabilizer
- Presence of mixed features is a predictor of lithium non-response
- Antidepressants should be avoided
- NOTE: so far, no studies have primarily enrolled individuals meeting criteria for mania with mixed features specifiers

### ACUTE MAJOR DEPRESSIVE EPISODES:
- Lithium, lamotrigine, quetiapine, olanzapine-fluoxetine, lurasidone
  - Last 2 may be used in Bipolar I and II
  - Quetiapine first line in bipolar II depression
- VPA cannot be used for depression monotherapy
- Aripiprazole and ziprasidone = negative results in bipolar depression

### DEPRESSIVE EPISODES WITH MIXED FEATURES:
- New DSM-V diagnosis = limited evidence
- Lurasidone and olanzapine +/- fluoxetine reported to have benefits in post-hoc analysis
- Antidepressant monotherapy in MDD with subsyndromal hypomania may be associated with higher rate of suboptimal therapeutic outcomes when compared to MDD without subsyndromal hypomania

### ANTIDEPRESSANTS AND MANIC SWITCH:
- Antidepressants should not be used as monotherapy
  - Studies demonstrate no improvement of depressive sx
  - Should be used in conjunction with mood stabilizer
- Risk of manic switch lower with SSRI or bupropion, higher with SNRI & TCA
  - Switch from depression to activated state may not be seen after 10 weeks of treatment
  - Mood dysregulation = classic hypomania or manic episode, worsening depression, emergence of dysphoria and irritability
  - D/C when worsening irritability/dysphoria, mixed sx, rapid cycling, emergence of polarity switch, lack of benefit

### TREATMENT OF ACUTE MANIA OR DEPRESSION EPISODES WITH PSYCHOTIC FEATURES:
- Psychotic symptoms are seen in both acute bipolar manic and depressive episodes
  - More common in bipolar mania
- Antipsychotics are recommended when psychotic features are present

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### CONTINUATION TREATMENT:
- Therapy continued 2-4 months following acute response (during which time the risk of relapse is high)
- Optimize treatment, prevent adverse reactions, ensure adherence, prevent polarity switching, or relapse

### MAINTENANCE TREATMENT:
- Once there is mood stability for approx. 3 months during continuation txt
- Focus on the continued improvement of functioning
- Ongoing use of acute/continuation medications
  - Least number of agents at minimum effective dosage
  - Monotherapy = ideal
  - NOTE: greater risk of recurrence when mood stabilizers are abruptly discontinued versus tapered
- Prophylaxis against future mood episodes
  - Not all agents are equal in their ability to prevent manic and depressive episodes
    - Quetiapine = best coverage
    - Lamotrigine = poor anti-manic but best for depression
- Most recent episode of polarity
- Polarity of “index episode” (first episode presented)
- More frequently presenting pole of illness
- +/- frequent, recent, or severe mania

### STRATEGIES TO CHOOSE MAINTENACE THERAPY:
- Select medications that have a low relative risk of weight gain and metabolic syndrome
- Maintenance dose should generally be no less than half of the initial clinically effective dose, as that can result in reduced effectiveness of relapse prevention