Bipolar Disorder: Review of Disease State and Treatment

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Learning Objectives

1. Describe the epidemiology, etiology/pathophysiology, clinical presentation and diagnosis, comorbidity, course and prognosis of bipolar disorder.

2. Discuss pharmacologic treatment options for bipolar disorder.
3. Explain treatment approaches to bipolar disorder, including treatment of acute mania, treatment of acute depression, and long-term maintenance treatment.
Introduction

- *Mood* – emotional state
- *Mood episode* – discrete period of mood disturbance
- *Mood disorder* – any of several mental disorders characterized by abnormalities of emotional state
Mood Episodes

- Manic episode – abnormally and persistently elevated, expansive, or irritable mood
- Hypomanic episode – less intense than mania; does not result in marked impairment in functioning, hospitalization, or psychosis
Mood Episodes

- Major depressive episode – depressed mood or loss of interest or pleasure
- Mixed features can apply to any of the episodes – think of it as the presence of some symptoms from the opposite polarity
Major depressive disorder

Bipolar I disorder
Bipolar Disorders

• Bipolar I disorder – one or more manic episodes (with or without a depressive episode)

• Bipolar II disorder – one or more hypomanic episodes and one or more major depressive episodes (but no manic episodes)
Bipolar Disorders

• Cyclothymic disorder – at least 2 years of numerous periods of hypomanic symptoms (but no hypomanic episode) and numerous periods of depressive symptoms (but no major depressive episode)

• Others, such as substance-induced, medical conditions, etc.
Epidemiology

• Lifetime prevalence approx. 1% for bipolar I disorder, 1% for bipolar II disorder, and 4-5% for entire bipolar spectrum

• Bipolar I disorder affects males and females equally; bipolar II disorder is more common in females
Epidemiology

• Females with bipolar I or II disorder are more likely than males to experience depressive symptoms
Etiology/Pathophysiology

• Genetic factors
  – First degree relatives of patients have a 7-fold risk of developing the disorder
  – Adoption studies show that risk is with biological rather than adoptive parents
  – Twin studies show concordance rate of approx. 70% monozygotic vs. 20% dizygotic

• Stressful life events
Etiology/Pathophysiology

- Neuroanatomical abnormalities
- Neurochemical abnormalities
- Second messenger system/signaling cascade dysregulation
- Neuroendocrine dysfunction
- Immune-mediated dysfunction
- Circadian dysfunction
Clinical Presentation of Mania

- Elevated or euphoric mood
- Irritability
- Lability
- Increased energy or hyperactivity
- Decreased need for sleep
- Increased or pressured speech
- Distractibility
Clinical Presentation of Mania

- Racing thoughts or flight of ideas
- Grandiosity
- Delusions and/or hallucinations
- Demanding, threatening, or aggressive
- Impulsivity
- Garish appearance
Diagnosis of Manic Episode

• Mood = elevated or irritable (and increased energy or activity)
• Time frame = at least 1 week
• Symptoms = at least 3 of DIG FAST (next slide)
• Impairment in functioning, need for hospitalization, or presence of psychotic symptoms
DIG FAST

- D  distractibility
- I  involvement/indiscretion
- G  grandiosity
- F  flight of ideas
- A  agitation/activity
- S  sleep (decreased need)
- T  talkativeness
<table>
<thead>
<tr>
<th>Emotional</th>
<th>Physical</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Sadness</td>
<td>• Fatigue</td>
</tr>
<tr>
<td>• Anxiety</td>
<td>• Sleep disturbance</td>
</tr>
<tr>
<td>• Guilt</td>
<td>• Appetite/weight changes</td>
</tr>
<tr>
<td>• Irritability</td>
<td>• Decreased libido</td>
</tr>
<tr>
<td>• Anger</td>
<td>• Aches and pains</td>
</tr>
<tr>
<td>• Feelings of hopelessness or helplessness</td>
<td></td>
</tr>
</tbody>
</table>
Clinical Presentation of Depression

Cognitive/Perceptual
- Poor concentration
- Slowed thinking
- Indecisiveness
- Impaired memory
- Self-criticism
- Suicidal thoughts
- Delusions
- Hallucinations

Behavioral
- Crying
- Social withdrawal
- Psychomotor changes
- Neglect of responsibilities
- Changes in appearance
Diagnosis of Major Depressive Episode

- Mood = depression or anhedonia
- Time frame = at least 2 weeks
- Symptoms = at least 5 of SIG E CAPS (next slide); 1 must be either depressed mood or anhedonia
- Clinically significant distress or impairment in functioning
SIG E CAPS

- S  sleep (↑↓)
- I  interest (↓)
- G  guilt/worthlessness
- E  energy (↓)
- C  concentration (↓)
- A  appetite (↑↓)
- P  psychomotor (↑↓)
- S  suicidality
Differential Diagnosis

- Major depressive disorder
- Anxiety disorders
- Substance use disorders
- ADHD
- Personality disorders
Comorbidity

- Anxiety disorders
- ADHD
- Disruptive, impulse-control, and conduct disorders
- Substance use disorders
- Serious and/or untreated medical conditions
Course

• Often a substantial delay between onset of illness and diagnosis
• Misdiagnosis is very common early in the illness
• Onset usually late adolescence to early adulthood; onset of mania after age 60 is more likely to be due to medical conditions or substances
Course

• Commonly a chronic relapsing and remitting condition

• Highly recurrent
  – 90% have at least 2 episodes
  – 80% have > 4 episodes
Course

- More than one-half of manic episodes occur immediately before a depressive episode
- Some patients continue to experience residual mood symptoms and functional impairment between episodes
Course

• Acceleration of episode frequency is common
• *Rapid cycler* – ≥ 4 mood episodes per year
  – Approx. 10-20% of patients
  – Women > men
  – Poorer prognosis; more difficult to treat
Prognosis

- Mortality
- Suicide
- Substance abuse
- Employment difficulties/disability
- Divorce
- Financial/legal problems
- Medication nonadherence
- Hospitalization
Question #1

• Which of the following symptoms would **NOT** be consistent with a manic episode?

A. Racing thoughts
B. Excessive speech
C. Hypersomnia
D. Impulsiveness
Question #2

• Most patients with bipolar disorder experience:
  A. Comorbid substance use or anxiety
  B. The rapid cycling form of the illness
  C. Initial mood episodes in their 40s
  D. Manic episodes only
Pharmacotherapy Options

- Lithium
- Anticonvulsants
  - Valproate
  - Carbamazepine
  - Lamotrigine
- Second generation antipsychotics
- Others – FGAs, BZDs, other anticonvulsants, antidepressants
# FDA-Approved Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mania</th>
<th>Depression</th>
<th>Maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lithium</td>
<td>√</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>Valproate</td>
<td>√</td>
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<tr>
<td>Carbamazepine</td>
<td>√</td>
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<tr>
<td>Lamotrigine</td>
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<tr>
<td>Aripiprazole</td>
<td>√</td>
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<tr>
<td>Asenapine</td>
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<td>Cariprazine</td>
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<tr>
<td>Lurasidone</td>
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<tr>
<td>Olanzapine</td>
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<tr>
<td>Olanz/fluoxetine</td>
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<tr>
<td>Quetiapine</td>
<td>√</td>
<td>√</td>
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<tr>
<td>Risperidone</td>
<td>√</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>√</td>
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</tr>
</tbody>
</table>
Lithium

• Efficacy
  – Very good antimanic, antidepressant, and maintenance effects; prevention of mania > depression
  – Associated with lower rates of suicide
  – Slower onset of action relative to VPA and SGAs (approx. 7-10 days in mania)
  – Less effective for patients with mixed features or rapid cycling
Lithium

• Adverse effects
  – Renal: polyuria, chronic kidney effects
  – CNS: tremor
  – GI: N/V/D
  – Endocrine/metabolic: weight gain, hypothyroidism, hyperparathyroidism
Lithium

• Adverse effects (cont.)
  – Cardiovascular: AV block/other conduction issues
  – Hematologic: leukocytosis (benign)
  – Dermatologic: acne, psoriasis, alopecia
  – Reproductive/pregnancy: teratogenicity
Lithium

• Toxicity
  – Lithium has a narrow therapeutic index
  – Signs and symptoms include coarse tremor, diarrhea, vomiting, and CNS symptoms such as confusion, dysarthria, and ataxia
  – Can be life-threatening
Lithium

• Drug interactions
  – NSAIDS, COX-2 inhibitors (↑ Li level)
  – Distal tubule diuretics (↑ Li level)
  – ACE inhibitors, ARBs (↑ Li level)

• Dosing
  – Initial dose: 300 mg bid or tid
  – Usual dose: 900-1,800 mg/day
  – Level: 0.6-1.2 mEq/L
Lithium

- Safety monitoring
  - Serum level
  - CBC
  - Electrolytes
  - Calcium
  - Creatinine/BUN
  - TSH
  - Weight/BMI
  - As clinically indicated: ECG, pregnancy
Valproate

• Efficacy
  – Indicated for mania, but good maintenance medication as well
  – Very good antimanic effects and some antidepressant effects; prevention of mania > depression
  – Effective in combination with lithium or SGAs
Valproate

• Adverse effects
  – GI: N/V/D, pancreatitis
  – Hepatic: elevated LFTs, hepatotoxicity
  – CNS: sedation, tremor, ataxia
  – Endocrine/metabolic: weight gain, hyperammonemia
  – Hematologic: thrombocytopenia
Valproate

• Adverse effects (cont.)
  – Dermatologic: alopecia, rash
  – Reproductive/pregnancy: menstrual irregularities, teratogenicity

• Drug interactions
  – Lamotrigine (↑ lamotrigine level)
  – Carbamazepine (↑ CBZ-epoxide levels; ↓ VPA levels)
Valproate

• Dosing
  – Initial dose: 250 mg bid or tid OR load with 20 mg/kg/day OR load with 30 mg/kg/day x 2 days, then decrease dose to 20 mg/kg/day
  – Usual dose: 1,000-1,500 mg/day
  – Max dose: 60 mg/kg/day
  – Level: 50-125 mcg/mL
Valproate

• Safety monitoring
  – Serum level
  – CBC
  – LFTs
  – Weight/BMI
  – As clinically indicated: menstrual history, pregnancy, ammonia level
Carbamazepine

• Efficacy
  – Indicated for mania
  – Good antimanic effects and some antidepressant effects; prevention of mania > depression
  – Not as commonly used as other mood stabilizers; usually reserved for patients who don’t tolerate or fail to respond to other mood stabilizers
Carbamazepine

• Adverse effects
  – CNS: dizziness, sedation, diplopia, ataxia, tremor
  – GI: nausea, vomiting, constipation
  – Hematologic: thrombocytopenia, neutropenia, agranulocytosis, aplastic anemia
  – Dermatologic: pruritus, rash, SJS/TEN
Carbamazepine

• Adverse effects (cont.)
  – Endocrine/metabolic: hyponatremia, weight gain
  – Hepatic: elevated LFTs, hepatotoxicity
  – Reproductive/pregnancy: teratogenicity
# Carbamazepine

## Drugs ↑ CBZ levels
- Valproate
- Fluoxetine
- Cimetidine
- Erythromycin
- Ketoconazole
- Verapamil, diltiazem

## CBZ ↓ levels of drugs
- Valproate
- Lamotrigine
- Antidepressants
- Antipsychotics
- Benzodiazepines
- Oral contraceptives
- Warfarin
Carbamazepine

• Dosing
  – Initial dose: 100-200 mg bid
  – Usual dose: 600-1,200 mg/day
  – Level: 4-12 mcg/mL (but no clear correlation with efficacy in bipolar disorder)
  – Adjustments may be necessary due to autoinduction
Carbamazepine

• Safety monitoring
  – Serum level
  – CBC
  – Electrolytes
  – LFTs
  – Rash
  – As clinically indicated: pregnancy, HLA-B*1502
Lamotrigine

• Efficacy
  – Indicated for maintenance treatment but used in acute depression as well
  – Good antidepressant effects, but no real antimanic effects; maintenance effects are more impressive, but prevention of depression > mania
Lamotrigine

- Adverse effects
  - Dermatologic: rash, SJS/TEN
  - GI: N/V/D
  - CNS: dizziness, headache, sedation, diplopia, ataxia
Lamotrigine

• Drug interactions
  – Valproate (↑ lamotrigine level)
  – Carbamazepine (↓ lamotrigine level)
  – Estrogen-containing products (↓ lamotrigine level)
Lamotrigine

• Dosing
  – Usual titration: 25 mg/day for 2 weeks, then 50 mg/day for 2 weeks, then 100 mg/day for 1 week, then 200 mg/day
  – Dosage adjustments: reduced dosages (approx. one-half) when given with valproate, and increased dosages (approx. double) when given with carbamazepine
Lamotrigine

• Safety monitoring
  – Rash
SGAs

• Efficacy
  – Various SGAs are FDA-approved for mania, depression, and maintenance (with or without Li or VPA)
  – SGAs vary in regard to efficacy in the various phases
    • Quetiapine – very good antimanic, antidepressant, and maintenance effects
SGAs

• Efficacy (cont.)
  • Aripiprazole, Risperidone, Ziprasidone – very good antimanic effects and very good at preventing mania; not useful for depression
  • Lurasidone – very good antidepressant effects; limited maintenance effects
SGAs

- Adverse effects
  - CNS: sedation, EPS
  - Endocrine/metabolic: weight gain, hyperglycemia, dyslipidemia, hyperprolactinemia
  - Cardiovascular: decreased blood pressure, tachycardia, QT prolongation
  - GI: dry mouth, constipation
SGAs

• Drug interactions
  – Various pharmacodynamic interactions
  – Most SGAs are CYP450 substrates, so metabolism can be influenced by various inducers and inhibitors
    • Ex: olanzapine levels can be decreased by carbamazepine
    • Ex: risperidone levels can be increased by fluoxetine
### SGAs

<table>
<thead>
<tr>
<th>SGA</th>
<th>Initial dose</th>
<th>Usual dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
<td>15 mg/day</td>
<td>15-30 mg/day</td>
</tr>
<tr>
<td>Asenapine</td>
<td>10 mg bid</td>
<td>5-10 mg bid</td>
</tr>
<tr>
<td>Cariprazine</td>
<td>1.5 mg/day</td>
<td>3-6 mg/day</td>
</tr>
<tr>
<td>Lurasidone</td>
<td>20 mg/day</td>
<td>20-120 mg/day</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>10-15 mg/day</td>
<td>5-20 mg/day</td>
</tr>
<tr>
<td>Quetiapine (mania)</td>
<td>50 mg bid or 300 mg qhs (XR)</td>
<td>400-800 mg/day given bid or hs (XR)</td>
</tr>
<tr>
<td>Quetiapine (dep)</td>
<td>50 mg qhs</td>
<td>300 mg qhs</td>
</tr>
<tr>
<td>Risperidone</td>
<td>2-3 mg/day</td>
<td>1-6 mg/day</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>40 mg bid</td>
<td>40-80 mg bid</td>
</tr>
</tbody>
</table>
SGAs

• Safety monitoring
  – Weight/BMI
  – Waist circumference
  – Blood pressure
  – Fasting glucose
  – Fasting lipids
  – Extrapyramidal side effects
  – As clinically indicated: ECG, prolactin
Other Medications

• First generation antipsychotics
  – Considered effective antimanic agents
  – Lack efficacy in maintenance treatment and may cause switch to depression
  – Not used nearly as much as SGAs

• Benzodiazepines
  – Adjunctive treatment in mania
Other Medications

• Other anticonvulsants
  – Oxcarbazepine: limited data supporting use in mania; some adv./disadv. relative to CBZ
  – Tiagabine, topiramate, zonisamide, gabapentin, levetiracetam: not recommended
Other Medications

- Antidepressants
  - Use is highly controversial
  - Antidepressants can cause mood switching and perhaps accelerate episode frequency or induce rapid cycling
  - As concerns drug classes, SNRIs and TCAs are most likely to cause mood switching
Other Medications

• Antidepressants (cont.)
  – Monotherapy should be avoided
  – Adjunctive therapy can be used:
    • Acute depression when there is a history of previous positive response
    • Maintenance treatment if depressive episodes occur after stopping antidepressants
Other Medications

• Antidepressants (cont.)
  – Adjunctive therapy should be avoided:
    • Manic or mixed states
    • Past history of mood switching during antidepressant treatment
    • High mood instability or rapid cycling
Which of the following OTC products is **MOST** likely to cause lithium toxicity if used concomitantly?

A. Tagamet HB  
B. Imodium  
C. Zyrtec  
D. Aleve
Question #4

• Routine long-term safety monitoring of olanzapine use in bipolar disorder would include which of the following?
  A. Liver function test
  B. Prolactin level
  C. Fasting glucose
  D. Thyroid stimulating hormone
Phases of Treatment

• Acute
  – Resolve current mood episode
  – Typical time frame for treatment response
    • Mania: within approx. 2 weeks
    • Depression: within approx. 4 weeks
Phases of Treatment

• Continuation
  – Prevent relapse or polarity switch
  – Approx. 3 months

• Maintenance
  – Prevent future mood episodes
  – Lifetime
# Treatment Guidelines

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>World Federation of Societies of Biological Psychiatry (WFSBP)</td>
<td>2009 (mania), 2010 (bipolar depression), 2012 (maintenance)</td>
</tr>
<tr>
<td>Canadian Network for Mood and Anxiety Treatments (CANMAT) &amp; International Society for Bipolar Disorders (ISBD)</td>
<td>2013</td>
</tr>
<tr>
<td>National Institute for Health and Care Excellence (NICE)</td>
<td>2014</td>
</tr>
<tr>
<td>British Association for Psychopharmacology (BAP)</td>
<td>2016</td>
</tr>
</tbody>
</table>
## Treatment Guidelines – Mania

<table>
<thead>
<tr>
<th>WFSBP</th>
<th>CANMAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Aripiprazole, Risperidone, Ziprasidone, VPA</td>
<td>Monotherapy: Li, VPA, Aripiprazole, Asenapine, Olanzapine, Paliperidone, Quetiapine, Risperidone, Ziprasidone</td>
</tr>
<tr>
<td>2 Switch to another 1st choice medication; consider combination in severe mania</td>
<td>Monotherapy: CBZ, haloperidol Combination therapy: Li + VPA</td>
</tr>
</tbody>
</table>
## Treatment Guidelines – Mania

<table>
<thead>
<tr>
<th>WFSBP</th>
<th>CANMAT</th>
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<tbody>
<tr>
<td>3</td>
<td>Combination treatment with 2 1&lt;sup&gt;st&lt;/sup&gt; choice medications</td>
</tr>
<tr>
<td></td>
<td>Various options including Chlorpromazine, Clozapine, Oxcarbazepine, others</td>
</tr>
<tr>
<td>4</td>
<td>Exchange one medication in step above with Li, CBZ, Haloperidol, Olanzapine, Quetiapine, others</td>
</tr>
</tbody>
</table>
## Treatment Guidelines – Mania

<table>
<thead>
<tr>
<th>NICE</th>
<th>BAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. If not taking mood stabilizer: Haloperidol, Olanzapine, Quetiapine, Risperidone. If taking Li or VPA: optimize treatment, then if insufficiently effective, consider adding one of the 1st line medications above.</td>
<td>Highest efficacy: Haloperidol, Olanzapine, Quetiapine, Risperidone. Alternatives: Li, VPA, CBZ.</td>
</tr>
<tr>
<td>2. Switch to another 1st line medication.</td>
<td>1st line medication + Li or VPA.</td>
</tr>
<tr>
<td>3. 1st line medication + Li or VPA (if Li is ineffective or unsuitable).</td>
<td></td>
</tr>
</tbody>
</table>
Treatment of Mania

- General conclusions from guidelines
  - 1st-line options: Li, VPA, and SGAs
  - 2nd- or 3rd-line options: CBZ, FGAs
  - Treatment-resistance: ECT, clozapine

- Combination therapy
  - Li or VPA + SGA
  - More effective than monotherapy
  - Especially in severe/psychotic cases
Treatment of Mania

- Antidepressants should be tapered and discontinued when possible
- Benzodiazepines can be used as short-term adjunctive treatment for anxiety, agitation, and insomnia
- Presence of mixed features
  - Predictor of non-response to Li
  - Should avoid antidepressants
## Treatment Guidelines – Depression

<table>
<thead>
<tr>
<th></th>
<th>WFSBP</th>
<th>CANMAT</th>
</tr>
</thead>
</table>
| 1 | Quetiapine, Olanzapine, Lamotrigine, Li, VPA, CBZ | Monotherapy: Li, Lamotrigine, Quetiapine  
Combination therapy: Li or VPA + SSRI or Bupropion, Olanzapine + SSRI, Li + VPA |
| 2 | Switch to or combine with another recommended medication | Monotherapy: VPA, Lurasidone  
Combination therapy: Li or VPA + Lamotrigine or Lurasidone, Quetiapine + SSRI |
| 3 | Consider various augmentation treatments, including antidepressants, modafinil, N-acetylcysteine, others | Various options including CBZ, Olanzapine, and numerous combinations |
## Treatment Guidelines – Depression

<table>
<thead>
<tr>
<th>NICE</th>
<th>BAP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1</strong> If not taking mood stabilizer: Olanzapine/Fluoxetine, Quetiapine, Olanzapine (alone), Lamotrigine If taking Li or VPA: optimize treatment, then if insufficiently effective, add one of the 1st line medications above</td>
<td>Lurasidone, Olanzapine, Quetiapine, Lamotrigine</td>
</tr>
<tr>
<td><strong>2</strong> Switch to Lamotrigine Lamotrigine + Li or VPA</td>
<td>Switch to another 1st line medication or combine 2 1st line medications Consider antidepressant + antimanic drug</td>
</tr>
<tr>
<td><strong>3</strong></td>
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</tbody>
</table>
Treatment of Depression

• General conclusions from guidelines
  – 1st-line options: Li, lamotrigine, quetiapine, lurasidone, olanzapine/fluoxetine (latter 3 are FDA-approved)
  – 2nd- or 3rd-line options: Antidepressants (along with mood stabilizer), VPA, CBZ
  – Treatment-resistance: ECT
Treatment of Depression

• Combination therapy
  – Two 1st-line medications
  – Especially after failed monotherapy

• APDs are recommended in psychotic cases

• Negative results with some SGAs (aripiprazole, ziprasidone)
## Treatment Guidelines – Maintenance

<table>
<thead>
<tr>
<th></th>
<th>WFSBP</th>
<th>CANMAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Aripiprazole, Quetiapine, Lamotrigine, Lithium</td>
<td>Monotherapy: Li, Lamotrigine, VPA, Aripiprazole, Olanzapine, Quetiapine, Risperidone LAI Adjunctive therapy: Li or VPA + Aripiprazole, Quetiapine, Risperidone LAI, or Ziprasidone</td>
</tr>
<tr>
<td>2</td>
<td>Olanzapine, Risperidone</td>
<td>Monotherapy: CBZ, Paliperidone Combination therapy: Li + VPA, CBZ, Lamotrigine, or Risperidone, Li or VPA + Olanzapine, Olanzapine + Fluoxetine</td>
</tr>
<tr>
<td>3</td>
<td>Paliperidone, Ziprasidone, Antidepressants, VPA</td>
<td>Various options</td>
</tr>
</tbody>
</table>
## Treatment Guidelines – Maintenance

<table>
<thead>
<tr>
<th>NICE</th>
<th>BAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Li</td>
<td>Li</td>
</tr>
<tr>
<td>2 If poorly tolerated or unsuitable: Olanzapine, Quetiapine, VPA If ineffective: Li + VPA</td>
<td>If poorly tolerated or unsuitable: VPA or APD If ineffective: Depression predominant? Li + Lamotrigine, Quetiapine, or Lurasidone Mania predominant? Li + VPA or APD</td>
</tr>
<tr>
<td>3</td>
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</tbody>
</table>
Maintenance Treatment

• General conclusions from guidelines
  – 1st-line options: Li, lamotrigine, VPA, SGAs (aripiprazole, olanzapine, quetiapine, risperidone, ziprasidone)

• Combination treatment
  – Li or VPA + SGA, Li + VPA
  – But monotherapy is ideal
Maintenance Treatment

• Medication selection
  – Influenced by patient’s illness pattern
  – Medications are different in their ability to prevent manic and depressive episodes

• SGAs have safety concerns in long-term use
Treatment Goals

• Resolve mood episodes
• Prevent future mood episodes
• Normalize functioning
• Minimize adverse effects
• Maximize medication adherence
Evaluation of Therapeutic Outcomes

• Mood charting
• Functional status
• Suicidality
• Frequency/severity of symptoms
• Formal rating scales (examples)
  – Mania: Young Mania Rating Scale
  – Depression: Hamilton Depression Rating Scale
Question #5

• Which of the following would be the **BEST** option after a trial of risperidone for treatment of acute mania is insufficiently efficacious?

A. Add ziprasidone
B. Add valproate
C. Switch to lorazepam
D. Switch to clozapine
Question #6

• All of the following would be good options for long-term maintenance treatment of bipolar disorder **EXCEPT**:  
  A. Fluoxetine  
  B. Lamotrigine  
  C. Lithium  
  D. Quetiapine
References

• Treatment guidelines
  – WFSBP: World Journal of Biological Psychiatry
References

– NICE: nice.org.uk/guidance/cg185
References

• Other guidelines
References

• Books/chapters
  – DSM-5: Diagnostic and Statistical Manual of Mental Disorders, 5th ed.
References

— Ott C. Bipolar disorder chapter of 2018-2019 CPNP BCPP Examination Review and Certification Course

— Kehoe WA. Psychiatric disorders chapter of ACCP Updates in Therapeutics 2017