

Bipolar Disorder

Mania and Hypomania

Prepared by: Dr. Anvesh Roy
Psychiatry Resident, University of Toronto

This is a review of Bipolar disorder focusing primarily upon its defining phenomena of Mania and Hypomania. The following text is envisioned to help case based learning of Bipolar Disorder by providing a background context (the video case). This is designed to show how the scenario may present in real life when you are faced with a similar patient rotating through the ER or in an inpatient unit.

Click on the following hyperlinks to arrive at each section with pertinent examples from our video case (commiserate to enabling objectives):

- [What is Mania and Hypomania?](#) Definition and meaning.
- [Differential Diagnosis](#)
- [How to get a history and pertinent information](#)
- [Objective evaluation: Physical Exam and MSE](#)
- [What are the investigations?](#)
- [Management](#)
- [Short Term](#), including addressing safety concerns and acute agitation
- [Long Term](#)
- [References](#) and further reading (for the so inclined)

What is Mania (and Hypomania)?

An extremely disabling and potentially harmful behavioral syndrome that indicates an underlying central nervous system disorder. Mania can lead to harm to self or others, and may be accompanied by features of psychosis. Hypomania is a less severe form of mania, see later on in the text how to differentiate between the two.

Usually, by definition they denote affliction by one of the various forms of Bipolar Disorders or 'Bipolar Spectrum' of disorders.

They can be secondary to other causes, but then they are not referred to as such, as will be explained.

DSM5 Dx Criteria:

Manic Episode

- A. A distinct period (at least one week) of abnormally/ persistently elevated, expansive, irritable mood and abnormally/persistent increased goal directed activity or energy; any duration is enough to diagnose if hospitalization required
- B. During this period, three or more of (or four if mood is irritable) as remembered by the mnemonic GSTPAID:
 - Inflated self-esteem or grandiosity - G
 - Decreased need for sleep - S
 - More talkative/pressure speech - T
 - Excessive engagement in activities with high potential for painful consequences - P
 - Increase in goal directed activity or psychomotor agitation - A
 - Flight of ideas or subjective racing thoughts - I
 - Objective or subjective distractibility - D
- C. Mood disturbance causes impairment in social occupational functioning OR necessitates hospitalization to prevent harm to self OR psychotic features
- D. Not attributable to a General Medical Condition or substance

Hypomanic Episode

- A. A distinct period (at least 4 consecutive days) of abnormally/ persistently elevated, expansive, irritable mood and abnormally/persistent increased goal directed activity or energy.
- B. During this period, **three or more of (or four if mood is irritable):**
 - a. Inflated self-esteem or grandiosity - G
 - b. Decreased need for sleep - S

- c. More talkative/pressure speech - T
- d. Excessive engagement in activities with high potential for painful consequences - P
- e. Increase in goal directed activity or psychomotor agitation - A
- f. Flight of ideas or subjective racing thoughts - I
- g. Objective or subjective distractibility - D
- C. Episode associated with uncharacteristic change in functioning
- D. Disturbance observable by others
- E. Not severe enough to cause marked impairment, no hospitalization required, no psychotic features
- F. Not attributable to substance

Major Depressive Episode

- Reviewed elsewhere on the HUB

Differential Diagnosis:

Bipolar Disorder

Bipolar disorder, or manic-depressive illness, is a mood disorder that is accompanied by extreme mood “swings” that differ significantly from normal mood variation. Bipolar disorder typically consists of three states:

- (1) a high state, called “mania”;
- (2) a low state, called “depression”; and
- (3) a well state, during which many people feel normal and function well. The manias and depressions may be “pure” episodes (containing only typical manic or depressive symptoms) or they may be with mixed features (containing a mixture of manic and depressive symptoms at the same time).

Epidemiology:

- Lifetime prevalence
 - Bipolar I: 0.5-2.4%; M=F
 - Bipolar II: 0.2-5.0%; F>M
 - Overall: 2-4%
- Onset of illness has two peaks: 15-19 yrs. and 40-50 yrs.
- Duration of untreated episodes:
 - Manic: 12 wks.
 - Depressive: 19 wks.

- Mixed: 36 wks.
- Average number of lifetime episodes is 7-9
- Bipolar II has higher risk of rapid cycling than Bipolar I (7:1 ratio), as well as a more chronic and recurrent course, with >50% of the time ill (mainly with depressions)

Mania and Hypomania can be present in the following disorders, and these are the diagnostic criteria as per DSM5:

A. Bipolar I

- need a current or past manic episode, likely will also have depressive episodes
- a full manic episode that emerges during antidepressant treatment (meds, ECT) but persists as fully syndromal level beyond physiological effect of that treatment IS SUFFICIENT EVIDENCE for a manic episode AND THEREFORE a bipolar I diagnosis
- not better explained by another diagnosis
- diagnostic code is based on CURRENT OR MOST RECENT episode and whether its severity, presence of psychotic features, and remission status
- bipolar I disorder, most current episode manic, severe, with psychotic features, in partial remission
- bipolar I disorder, most recent episode depressed, mild, in full remission
- code psychotic features irrespective of severity

B. Bipolar II

- Need a current or hypomanic episode AND current or past depressive episode, AND LACK of a manic episode
- a full hypomanic episode that emerges during antidepressant treatment (meds, ECT) but persists as fully syndromal level beyond physiological effect of that treatment IS SUFFICIENT EVIDENCE for a manic episode AND THEREFORE a bipolar II diagnosis
- caution if just one or two symptoms like edginess, irritability or agitation following antidepressant initiation – not a bipolar diathesis
- not better explained by another diagnosis
- diagnostic code is disorder, current /recent episode, presence of psychotic features, course, and other specifiers
- bipolar II disorder, current episode depressed, moderate severity, with missed features

C. For both bipolar I and II, one can add specifiers

- anxious distress

- mixed features
- rapid cycling
- melancholic features
- atypical features
- mood-congruent psychotic features
- mood-incongruent psychotic features
- catatonia
- peripartum onset
- seasonal pattern – only apply to pattern of depressive episodes

Cyclothymic Disorder: a chronic, fluctuating mood disturbance

- A. Two years in adults/one in children - Numerous periods with hypomanic or depressive symptoms
- B. Hypomanic or depressive symptoms present at least half of the time and individual not without symptoms for more than two months
- C. Not meeting full syndromal criteria for either hypomania or depression EVER
- D. Not better explained by other disorder
- E. Not attributable to substance or GMC
- F. Impairment

Substance/Medication-Induced Bipolar and Related Disorders

- A. Prominent and persistent mood disturbance characterized by elevated, expansive, irritable mood – with or without depressed mood OR markedly diminished interest or pleasure in almost or all activities
- B. Evidence that these symptoms developed during or soon after exposure/intoxication/withdrawal of a substance that is capable of producing these symptoms
- C. Not better explained by bipolar disorder or non-substance diagnosis
- D. Not only in delirium
- E. Impairment
 - Code use disorder prior to substance-induced diagnosis and onset during intoxication/withdrawal
 - Amphetamine-induced bipolar and related disorder, with onset during intoxication
 - Severe methylphenidate use disorder with methylphenidate-induced bipolar and related disorder, with onset during intoxication

Bipolar and Related Disorders Due to Another Medical Condition

- A. Prominent and persistent mood disturbance characterized by elevated, expansive, irritable and abnormally increased activity and or energy

- B. Evidence that disturbance is the direct pathophysiological consequence of medical condition
- C. Not better explained another mental disorder
- D. Not only in delirium, although delirium may present with manic like symptoms
- E. Impairment
 - Specific: with manic features, manic/hypomanic-like episode, with mixed features

Other Specified Bipolar and Related Disorders

- Short-duration hypomanic and major depressive episodes – 2-3 days
- Hypomanic episodes with insufficient symptoms and major depressive episodes
- Hypomanic episode without prior major depressive episode
- Short duration cyclothymia – less than 24 months

Unspecified Bipolar and Related Disorders

- Presentation with characteristic symptoms that cause distress, but do not meet criteria and sufficient information not available.

Schizoaffective Disorder

- A. Major mood episode (depression/mania) concurrent with Criterion A of Schizophrenia
- B. Delusions/hallucinations present for atleast 2 or more wks. in ABSENCE of major mood episode during the lifetime of the patient.
- C. Sx that meet criteria for a major mood episode present for majority of total duration of active and residual portions of illness.
- D. Not secondary to substance or another GMC.

Specifiers:

Bipolar type

Depressive type

With catatonia

Important diagnostic points:

- The key difference between mania and hypomania is that mania is associated with significant social or occupational dysfunction whereas hypomania is not. There are also no psychotic features in Hypomania. The minimum duration also differs 4 vs. 7 days.
- A mania and hypomania due to the Bipolar Spectrum of Disorders can be diagnosed if precipitated by a substance or medication – and it persists beyond the physiological effect of intoxication or withdrawal syndrome of the substance. For e.g. An SSRI precipitates a manic episode, and this episode persists for more than a week after the SSRI is stopped.
- Mixed episode used to be a separate entity in DSM IV but in DSM5 it is a specifier and denotes symptoms of depression co-occurring with the manic or hypomanic episode.
- Psychotic symptoms (e.g., delusions, hallucinations) are common in mania, appearing in over one half of manic episodes. In manic states, patients often experience grandiose and paranoid delusions, as well as perceptual abnormalities, resulting in visual, auditory, and olfactory experiences
 - The psychosis is likely to be ‘mood congruent’ i.e. goes along with the elevated mood and grandiosity or themes of increased energy or power. As seen in the case – pt. feels that she will cause world war 3, as she is the most beautiful woman in the world.

Common Substances and Medical Conditions causing Mania

(From K & S 10th Ed.)

Amphetamines

Baclofen

Bromide

Bromocriptine

Captopril

Cimetidine

Cocaine

Corticosteroids (including adrenocorticoid hormone [ACTH])

Cyclosporine

Disulfiram

Hallucinogens (intoxication and flashbacks)

Hydralazine

Isoniazid

Levodopa

Methylphenidate

Metrizamide (following myelography)
Opiates and opioids
Phencyclidine (PCP)
Procarbazine
Procyclidine
Yohombine

Table 2
Selected Causes of Secondary Mania

Medical Conditions

- Brain tumors
- Strokes
- Traumatic brain injury
- Psychomotor seizures
- Multiple sclerosis
- Huntington disease
- CNS infections (including HIV)
- Hyperthyroidism
- Hyperadrenalism

Medications

- Anabolic steroids
- Antidepressants
- Cocaine
- Corticosteroids/corticosteroid withdrawal
- Dextromethorphan
- Dopamine agonists (eg, amantadine, bromocriptine, levodopa)
- Hypericum (St. John's wort)
- Isoniazid
- Stimulants
- Sympathomimetic amines (eg, ephedrine)
- Zidovudine

CNS=central nervous system; HIV=human immunodeficiency virus

Levenson JL. *Primary Psychiatry*. Vol 12, No 8. 2005.

How to gather pertinent history?

Conduct an interview

(Please refer to the video demonstration of the interview)

General interviewing tips for interviewing a pt. with mania/hypomania:

- When interviewing an acutely manic patient, you need to maintain a flexible approach. A controlled, ordered, sequential assessment is highly unlikely to flow, due to the patient's own disorganized thought form and behavior.
- It is essential to gain as much collateral information as possible when interviewing the acutely manic patient. It is sometimes useful to gain collateral information before interviewing the patient, particularly in emergency assessments.
- Do not engage in conversation of a personal nature, as it relates to you, with the manic patient. Calmly redirect the conversation back to the pertinent history of the patient.
- Patients with mania are often extremely distractible and stimulus bound, and by using clear questions and simple language that require short answers
- High yield and specific themes in mania are often to do with increased activity, energy and creativity with a 'flight of ideas' that may become disjointed and disorganized as the severity increases. Also, increased spending and sexuality and other indiscretions are quite dramatic and strong clinical clues.
- One cannot understand pt.'s interest in daily activities without understanding her at baseline. Only then can you interpret whether her mood is affecting her baseline level of functioning.
- Ask about treatment response to various drugs/mood stabilizers tried in the past.
- If you encounter someone with antidepressant-induced mania, search very carefully for evidence of spontaneous episodes.
- It is important to ask about symptoms of depression. This is to rule out a mixed episode and also to see if there were prior episodes.
- Ask about current stressors
- Also make sure patient isn't neglecting self-care due to intense manic symptoms.
- Establish the course of illness – number of manic or depressive episodes, their duration and their nature/impact on pt.'s life.
- Ask also about:
 - Other Psychotic symptoms e.g. Hallucinations, other delusions (see in psychosis section)
 - Substance use history, esp. stimulants drugs.
 - Establish a temporal relationship of drugs to manic symptoms
 - **Safety assessment – Suicide and Homicide**
- Ask about child-care responsibilities or driving.
- Inquire into current and past medical history to rule out medical/iatrogenic causes of mania (for e.g. Prescription steroids).
- Ask about family history of Bipolar disorder

Obtain Collateral History

The observations of a third party can be invaluable. This is particularly so for issues that patients themselves may have difficulty describing, or may not be aware of, such as: type of onset and evolution overtime, what actual changes have occurred (e.g., in personality and functioning), self-care issues, or fluctuations in state.

Case Notes:

Background Information (provided in as the nurse's report):

- Catie is a 32 y.o female
- Currently single, divorced 4 years ago, no children
- Works in retail in a fashion store
- Brought to the ED by her sister, who was concerned about her behavior and excessive spending. Told the triage nurse that her sister had 'Manic Depression' and left suddenly.

The following history was obtained from a discharge summary when the patient was admitted to the hospital 2 years ago.

It is estimated by her sister that she has been non compliant with her medications for about 2-3 weeks.

Past Psychiatric History:

3 prior hospitalizations. The first was 10 years ago where she presented in a manic state and was diagnosed with Bipolar Type 1. The other two ones were for Mania 5 years ago and Depression 2 years ago (this hospital) respectively. She has been known to be noncompliant with her medications.

Medications (last known 2 years ago)

Lithium 1200mg QHS
Bupropion 300mg QHS

Past Medical History:

- None

Family History:

- Grandmother – suspected Bipolar D/O
- Mother – Bipolar D/O on Lithium
- Reports of an Aunt and two maternal cousins with Bipolar Disorder

Social History:

- Unremarkable, normal milestones
- Grade A student until University, had to drop out due to first episode of Mania

- Employed in retail fashion
- Married for 2 years. Reason for divorce was apparently spending couples savings on luxury items amounting to 50000\$ and having an affair when she was in a Manic Episode.

Mental Status findings in Mania and its interpretation:

Appearance can be with flamboyant and/or sexually provocative dressing and makeup. Behavior can be hyperactive. Speech is pressured and with an increased rate, often loud. Mood is usually described as great or happy and affect is usually elevated, expansile or euphoric. It can also be irritable and also labile i.e. shift rapidly between all these states. Moreover, the mood is usually not appropriate to the situation. Thought process can be disorganized and sped up as reflected by rapid speech with a 'flight of ideas', which may be connected thematically and less so as the severity of mania increases. Thought content usually has grandiose delusions or others (in mania, not in hypomania). Perception may have hallucinations (in mania). Insight and Judgment may be very poor.

Physical exam may have to be deferred, however, take vital signs and perform an exam as clinically indicated. For e.g. Cocaine induced manic symptoms may have additional findings of a very elevated BP and pulse, which would need to be further investigated with an ECG and medical consult. At worst, this pt. may be having an MI.

Case Notes:

MSE exam is documented in the chart. It reads: Ms. Catie Holmes is a 32 y.o female who appears her stated age. Appearance is remarkable for wearing revealing and likely designer clothes with excessive makeup. Behavior is hyperactive and agitated at times. Speech is pressured and with an increased rate, often loud. Mood is described as 'happy and on top of the world' and affect is elevated and euphoric. Not appropriate to situation. It is also irritable in parts and quite labile. Thought process is disorganized with apparent flight of ideas connected to grandiose delusional themes. There is no suicidal or homicidal ideation. Thought content has grandiose delusions. Perception appears normal. Insight is poor and Judgment is quite poor – wants to fly to Milan in this state which can lead to unfortunate outcomes. Also, pt. is exercising poor judgment with finances.

What are the Investigations?

Suggested medical workup for secondary mania/hypomania:

Laboratory studies could include blood chemistry, complete blood cell count, liver function test, thyroid function tests, erythrocyte sedimentation rate, blood cultures, cortisol levels, HIV test, urine analysis, and urine drug screen.

Additional testing may be recommended, if indicated, depending upon the presentation and differential diagnosis. Imaging studies include CT or MRI brain scan, electroencephalogram, x-ray, and lumbar puncture, among any other clinically relevant studies.

Order drug levels if pt. is on a mood stabilizer. For Lithium order thyroid and renal tests. For Valproate and Carbamazepine, order LFTs.

Case Notes:

Catie's lab and other results:

- Urine Drug Tox negative
- Physical exam by ER MD was reported as "normal"
- Initial blood work (CBC, lytes) "normal" TSH pending
- Lithium level is 0
- Pregnancy urine test negative

What is the Management?

Continue to obtain collateral information

Establish a diagnosis and management plan

Explain this to the pt. in a non-confrontational and respectful manner (if possible)

Address medical concerns

If pt. needs hospitalization – assess if this will be voluntary or involuntary

A short term and long term management plan

Think bio-psycho-social:

Short term:

Assess if pt. meets criteria for certification (see Legal section of HUB for details)

Usually Form 1 is required if pt. is reasonably at risk for

- Self harm (imminent)

- Violence to others (imminent)
- At risk for physical impairment i.e. lack of self care to the point that it becomes a danger to the pt. for e.g. the pt. provokes others into a fight due to their irritable state

Depends on level of agitation or need for emergency measures at any point, this is similar to the management of a psychotic pt. if the mania is very severe with psychosis. Refer to that section for details of management and chemical restraints.

A note about Safety:

Always remember that safety is first. If at any point during the interview or later you feel threatened, leave the room and ask for assistance. The assessment can be finished with the help of a nurse, PA or security. At other times, the patient is so agitated that an emergency chemical restraint is necessary before assessment can be completed for the safety of the patient and medical personnel. The assessment may also have to be deferred. However, try to ask questions re SI/HI or other pertinent safety risks in order to be able to make a clinical decision.

Make sure there are no acute medical concerns requiring further assessment and treatment e.g. acute delirium secondary to a toxic substance with unstable vitals

Case Notes:

The psychiatrist offers Catie some PRN medication after explaining the diagnosis calmly. Catie gets very agitated demanding to leave for Milan for her photo shoot. A code white is called and PRN meds are offered orally at first. She refuses even after repeated attempts to convince her. At this point she had to be mechanically restrained and treated with IM Olanzapine 5mg and Ativan 2mg IM.

After 30 mins, a Form 1 is filled out and a Form 42 given to Catie, advising her she needs to stay involuntarily upto 72 hours as she is at a risk for physical impairment to herself. She may go the airport in this state and may be accosted by the authorities or meet with a violent incident attempting to fly in this state. She accepts this calmly, as she is quite sedated.

Assess capacity – usually done after acute stabilization

For mania/hypomania doing a Financial Capacity assessment if often necessary and it is the duty of the attending physician to do so. This is to protect the pt. from losing their money due to spending/investing in a manic state. A Form 21 (Certificate of Incapacity for managing property) needs to be filled out and a notice delivered to pt.

If pt. is voluntary or involuntary and capable (for treatment decisions) – go ahead and treat with informed consent

If involuntary, assess need for a Form 3 (involuntary hospitalization upto 2 weeks) as Form 1 expires in 72 hours. Get patient rights advice.

If incapable for treatment decisions do a Form 33 and apply for rights advice and find a SDM

If the patient challenges Form 3 and/or 33 and/or 23, prepare and participate in a Consent and Capacity Board hearing and abide by its decision.

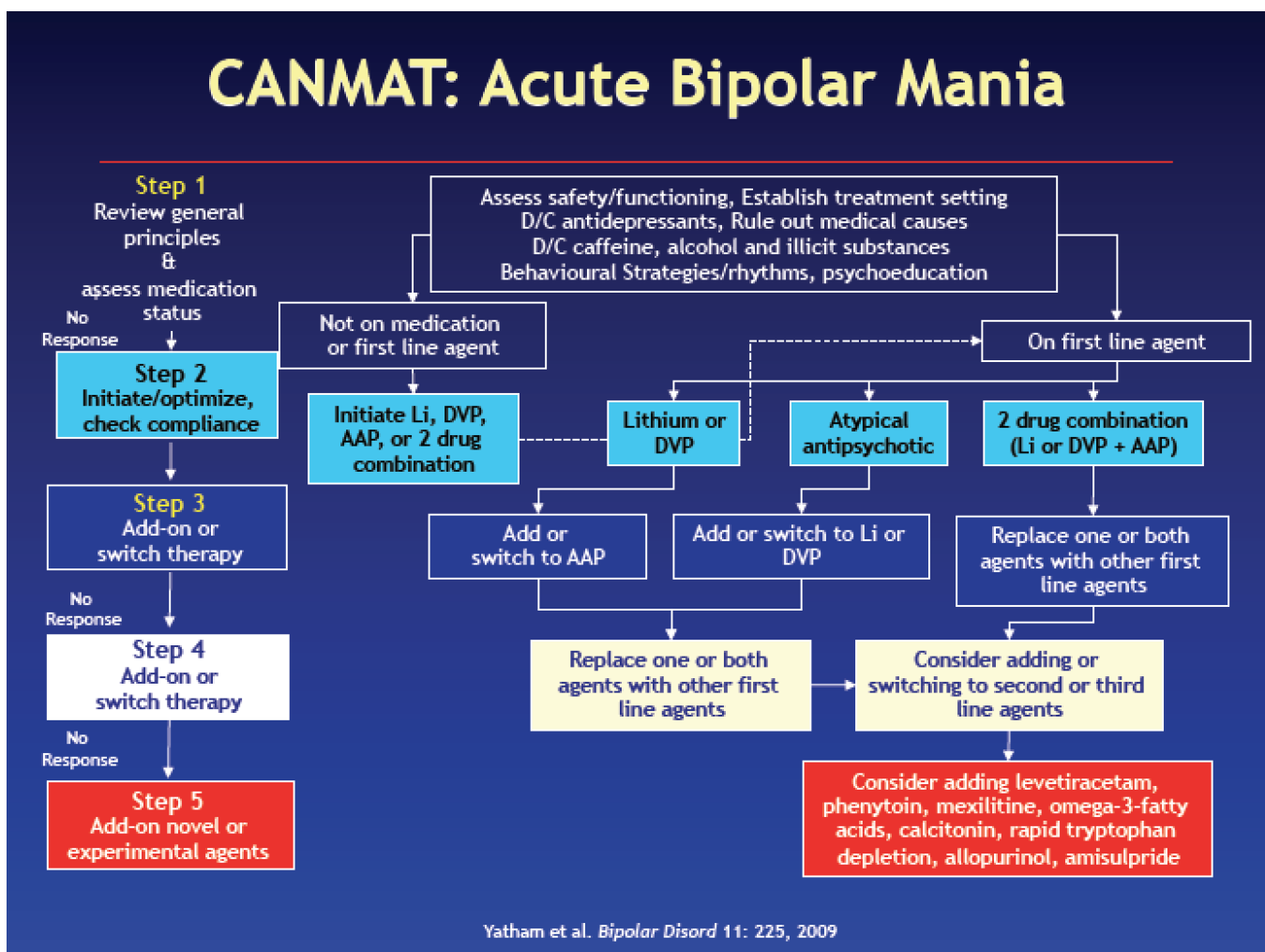
Ensure ongoing assessment of capacity and the need for a substitute decision-maker

Attend to the patient's immediate psychosocial needs e.g. contacting family, legal requirements etc. Can involve social worker.

Counsel and support patient/caregiver/family regarding clinical impression/management

Refer the patient for specialized care once stabilized e.g. Bipolar Disorder Clinic or First Episode bipolar Disorder clinic.

Psychopharmacology for Acute Management of Mania:



CANMAT 2012: Acute Mania


First line	<u>Monotherapy</u> : lithium, divalproex, divalproex ER^a , olanzapine ^b , risperidone, quetiapine, quetiapine XR, aripiprazole, ziprasidone, asenapine^a , paliperidone ER^a <u>Adjunctive therapy with lithium or divalproex</u> : risperidone, quetiapine, olanzapine, aripiprazole, asenapine^a
Second line	<u>Monotherapy</u> : carbamazepine, carbamazepine ER, ECT, haloperidol^a <u>Combination therapy</u> : lithium + divalproex
Third line	<u>Monotherapy</u> : chlorpromazine, clozapine, oxcarbazepine, tamoxifen, cariprazine^a (not yet commercially available) <u>Combination therapy</u> : lithium or divalproex + haloperidol, lithium + carbamazepine, adjunctive tamoxifen
Not recommended	<u>Monotherapy</u> : gabapentin, topiramate, lamotrigine, verapamil, tiagabine <u>Combination therapy</u> : risperidone + carbamazepine, olanzapine + carbamazepine

ECT = electroconvulsive therapy; XR or ER = extended release.

^aNew or change to recommendation.

Yatham et al. *Bipolar Disord* December 2012 Epub

Long Term and maintenance therapy for Bipolar Disorder:



Maintenance Pharmacotherapy

1 st line	2 nd line	3 rd line
<ul style="list-style-type: none">• Lithium• lamotrigine monotherapy (limited efficacy in preventing mania)• Divalproex• Olanzapine• Quetiapine• lithium or divalproex+ quetiapine^a• risperidone LAI^a• adjunctive risperidone LAI,^a• aripiprazole (mainly for preventing mania)^a• adjunctive ziprasidone^a	<ul style="list-style-type: none">• Carbamazepine• lithium + divalproex• lithium + carbamazepine• lithium or divalproex + olanzapine• lithium + risperidone• lithium + lamotrigine• olanzapine + fluoxetine	<ul style="list-style-type: none">• Adjunctive phenytoin• adjunctive clozapine• adjunctive ECT• adjunctive topiramate• adjunctive omega-3-fatty acids• Adjunctive oxcarbazepine, or• adjunctive gabapentin

Not Recommended:
Adjunctive flupenthixol, monotherapy with gabapentin, topiramate or antidepressants

ECT=electroconvulsive therapy, LAI=long acting injection, SSRI=selective serotonin reuptake inhibitor.

Canadian Network for Mood and Anxiety Treatments (CANMAT) guidelines for the management of patients with bipolar disorder: Update 2009. Yatham et al. Bipolar Disorder 11, 225.

Please refer to CANMAT guidelines for an exhaustive review.

Psychotherapy and Social interventions:

- Active outreach of patients known to be more severely ill or noncompliant
- Encouraging patient to become actively involved in self-management
- Designing a relapse drill (create document with early relapse signs, self-treatment manoeuvres, pre-negotiated treatment approaches)
- Stress-management techniques (sleep regulation, avoidance of substance misuse)
- Involvement of family and key friends
- Connecting patient to other community resources to enhance support and autonomy

- Upto 50% pregnancies unplanned, important that women with bipolar disorder receive education early
- Adjunctive psychosocial therapies should be considered early in the course of illness
- Recommended that all patients first receive psycho-education (group or individual)
- Evidence that CBT, IPS-RT (Interpersonal Social Rhythm Therapy), and family interventions all improve outcome (reduction in hospitalizations and symptoms).

CBT shown to

- Increase adherence
- Improve functioning
- Reduce relapse
- Reduce need for Rx
- Reduce mood fluctuations
- Reduce hospitalization

IPS-RT shown to

- Reduces sub-syndromal symptoms
- More time euthymic and less time depressed
- Did not change relapse risk
 - Family therapy
- Reduces relapses and hospitalizations
- Improves depressive symptoms
- Improves Rx adherence

Case Notes:

Catie is admitted and then put on a Form 3 and is found incapable of treatment decisions after suitable assessment. A Form 21 is also done after discovering she had maxed out her credit cards buying a first class ticket to Milan and designer clothes. She appeals to the CCB where Form 3 and Treatment incapacity is upheld, but she wins the financial incapacity appeal.

Her Bupropion is discontinued and Lithium restarted and titrated to a blood level of 1.0. Quetiapine XR is added and titrated to a dose of 400mg. After 3 weeks there is considerable improvement. She is worried about the wasted money and says she does not remember the events of the past week or so. She regains her insight and treatment capacity. She agrees to follow-up with her Psychiatrist. She wants a note for work. She is grateful for the help she received. She reunites with her sister and thanks her for bringing her in.

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5. CANMAT guidelines for Bipolar disorder. 2013 update. Yatham et al.
6. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)