Bipolar Disorder

Screening and Management

Pass These and we're done!

* A 30 year old male was brought to the emergency room by the Police after was found wandering naked on the street. Patient was very irritable and resisted physically the officers' attempts to restrain him. In the ER presents very distractible, has poor attention, thinks he receives mental messages from Elvis Presley, his speech is very pressured. Stated he has not slept in days, has been having increased energy for at least 1 week

The most likely diagnosis is

A. Psychotic Episode

B. Depressive episode

C. Manic episode

D. Hypomanic episode

* 30 y/o female brought in to your office by her husband after 4 days of elated mood, decreased sleep, writing excessively, racing thoughts. Patient presents dressed in a bright red dress, with excessive makeup, making jokes, talking a lot. States she feels fine, there's nothing wrong with her and came only because her husband insisted for her to come. Has been going to work as usual and performing all her duties.

The most likely diagnosis is

A. Psychotic episode
B. Depressive episode
C. Manic episode
D. Hypomanic episode

* A 30 year old male was brought to the emergency room by the Police after was found wandering naked on the street. Patient was very irritable and resisted physically the officers' attempts to restrain him. In the ER presents very distractible, has poor attention, thinks he receives mental messages from Elvis Presley, his speech is very pressured. Stated he has not slept in days, has been having increased energy for at least 1 week. **In the past was treated for depression 2 times and was hospitalized after suicide attempt.**

The most likely diagnosis is

A. Recurrent Depression
B. Cyclothymia
C. Bipolar II
D. Bipolar I

* Which of the following medications is known to increase the risk of neural tube defects in the fetus, if administered to the mother during the first trimester of pregnancy?

A. Diazepam
B. Valproic acid
C. Paroxetine
D. Thiothixene
E. Lithium carbonate

* A 37y/o MWM comes to the office at his wife's urging. A few years earlier had a thyroid mass removed after which he developed mood changes with 25days of remarkable energy, hyperactivity and euphoria followed by several days of depressive symptoms. Following the depressive episode patient would have a few normal days then the manic symptoms would resume. The depressive episodes have variable duration of 1-2 weeks. This pattern continued to present time. Patient denies drug use and states his most recent lab results showed mild hypothyroidism. Patient gives a history of poor compliance with Lithium, neuroleptics and antidepressants. The best treatment for this patient at this time is:

A. Lithium
B. ECT
C. Valproic acid or Lamotrigene
D. TCA
E. Clozapine

Bipolar Disorder

* History
* Diagnosis
    * Types
    * Screening instruments
    * Differential Diagnosis
* Epidemiology/Course/Prognosis
* Treatment Options
* Medications
* Other Therapies
    * Psychological
    * Somatic
* Controversies

History

* Old Testament - depressive do
* Homer's "Illiad" –Ajax's suicide
* Hippocrates 400b.c. – *mania* and *melancholia*
* Aulus Cornelius Celsus (30A.D.) – *melancholia*
* Moses Maimonides (12th century physician)– *melancholia* - discrete disease entity
* 1686 – Bonet –*maniaco-melancholicus*
* 1850's – Jules Falret *-Folie circulaire*
* 1850's –Jules Baillarger –*folie a double forme*
* 1882- Karl Kahlbaum – *cyclothymia*
* 1899 -Emil Kraepelin – *manic–depressive psychosis*

You can't have it all!

"It isn't possible to get values and color. You can't be at the pole and the equator at the same time. You must choose your own line, as I hope to do, and it will probably be color."

DIAGNOSIS

* Major Depressive episode
* Manic Episode
* Mixed Episode
* Hypomanic Episode

* Bipolar I
* Bipolar II
* Bipolar NOS
* Cyclothymic Disorder
* Mood Disorder due to GMC
* Substance Induced Mood Disorder

Bipolar Disorder

* Significant functional impairment
* Bipolar I people go through cycles of major depression and mania
* Bipolar II similar to Bipolar I except that people have hypomanic episodes, a milder form of mania
* Rapid cyclers

Mood history

* Mania
    * Giddy, goofy, laughing fits, class clown
    * Explosive (how often, how long, how destructive and aggressive)
    * Irritable, cranky, angry, disrespectful, threatening
    * Grandiosity may present as EXTREME defiance and oppositionality
* Depression
    * Low frustration tolerance, self-destructive, no pleasure, lower level of irritability

CLINICAL FEATURES

* Manic Episode
  * Elated /expansive/irritable mood
  * Hyper verbal, gambling, ETOH
  * Clothing –bright colors
  * Impulsive
  * Religiously, sexually, persecutory preoccupations
  * Delusions
  * Regressed behaviors at times
* Coexisting Disorders
  * Anxiety
  * ETOH/Drug dependence
  * Medical conditions

MANIC EPISODE	HYPOMANIC EPISODE
>1 week of Elated, Expansive or Irritable mood	**4 days or more of Elated, Expansive or irritable mood**

3 or more (4 if mood is irritable):

DIG FAST
Distractibility, poor attention
Indiscretion, pleasurable activities
Grandiosity , inflated self esteem
Flight of ideas, Racing Thoughts
Activity increased, Psychomotor agitation
Sleep reduction
Talkativeness (pressured speech)

MANIC EPISODE	HYPOMANIC EPISODE
Marked impairment in functioning or hospitalization or psychotic features	**CHANGE (observable by others) in functioning, no hospitalization, no psychotic features**

Sx not due to substance or GMC

Diagnosis

MIXED episode	Major Depressive episode
1 week or more, manic and major depressive episode	2weeks of Depressed mood or loss of interest or pleasure
	4 or more: **S** leep changes **I** nterest (loss) **G** uilt (worthless) **E** nergy (lack) **C** ognition/**C** oncentration **A** ppetite **P** sychomotor agitation/ retardation **S** uicide/death preocp.

Marked impairment in functioning or hospitalization or psychotic features; Sx not due to substance or GMC

Bipolar Disorders

DISORDER	Mania	Depression
SINGLE MANIC EPISODE	**Manic sx**	**NONE**
BIPOLAR I	MANIA OR MIXED episode	NOT REQUIRED but typical
BIPOLAR II	HYPOMANIA but no mania or mixed episode	History of Major depressive episode
Cyclothymic 2 years or more of … <2mo w/o sx	hypomanic episodes No manic episode during first 2 years of illness	Depressive sx but not Major depressive episode during first 2 yrs
Bipolar NOS Duration < ?primary/substance/ GMC	Mania , mixed, hypomanic but no DX of Bipolar I/II/ or cyclothymia	Not required

Bipolar Disorders (cont)

Disorder	Manic sx	Depressive sx
Mood do. due to GMC - evidence of GMC (HX, PE, Labs) -not exclusively during Delirium	Manic, Mixed features	Depressive features
Substance induced mood do. -Sx start <1month of Ix/WD - evidence of Substance Ix/WD (HX, PE, Labs) - not exclusively during Delirium	Elevated, expansive or irritable	Depressed mood or anhedonia
Mood do. NOS		

A Quick Way to Think about it

* **_M_**ania and **_D_**epression: Bipolar I
* **_m_**ania and **_D_**epression: Bipolar II
* **_M_**ania and **_d_**epression: Bipolar NOS
* **_m_**ania and **_d_**epression: Cyclothymia

Screening Tools

Two Major Instruments

Sensitivity and specificity of the Mood Disorder Questionnaire for detecting bipolar disorder.

[1]Bipolar Disorder Research Program, Cambridge Hospital, Cambridge, MA 02139, USA.

* **OBJECTIVE:**

This study aims to replicate the sensitivity and specificity of the Mood Disorder Questionnaire (MDQ) for bipolar disorder and assess the impact of insight on the MDQ's sensitivity. Unlike prior telephone-based validation, this is the first clinical study to assess the validity of the MDQ.

* **METHODS:**

37 consecutive patients with bipolar spectrum illness received the MDQ, as well as 36 consecutive patients with unipolar depression. MDQ diagnoses were compared to DSM-IV-based SCID diagnoses. A total of 16 bipolar patients also received the Scale to Assess Unawareness of Mental Disorder (SUMD) to measure insight.

* **RESULTS:**

Overall sensitivity for the MDQ was 0.58, higher in bipolar I disorder (0.69) than in bipolar II/NOS (0.30, P=0.06). The sample was highly insightful, but the two patients with lowest insight both had false negative screens. Patients' low ratings of severity of mania (question 3 of the MDQ) explained almost half of all false negative results. Specificity was 0.67.

* **CONCLUSIONS:**

The MDQ demonstrates good sensitivity in insightful patients with bipolar I disorder, but may be less useful in patients with impaired insight or milder bipolar spectrum conditions

Mood Disorders Questionnaire

INSTRUCTIONS: PLEASE ANSWER EACH QUESTION AS BEST YOU CAN. UPON COMPLETING THIS FORM, PRINT YOUR COMPLETED FORM AND TAKE IT TO YOUR HEALTH CARE PRACTITIONER. HAS THERE EVER BEEN A PERIOD OF TIME WHEN YOU WERE NOT YOUR USUAL SELF AND (WHILE NOT USING DRUGS OR ALCOHOL) ...

	Yes	**No**
...you felt so good or so hyper that other people thought you were not your normal self, or you were so hyper that you got into trouble?		
...you were so irritable that you shouted at people or started fights or arguments?		
...you felt much more self-confident than usual?		
...you got much less sleep than usual and found you didn't really miss it?		
...you were much more talkative or spoke faster than usual?		
...thoughts raced through your head or you couldn't slow your mind down?		
...you were so easily distracted by things around you that you had trouble concentrating or staying on track?		
...you had much more energy than usual?		
...you were much more active or did many more things than usual?		
...you were much more social or outgoing than usual; for example, you telephoned friends in the middle of the night?		
...you were much more interested in sex than usual?		
...you did things that were unusual for you or that other people might have thought were excessive, foolish, or risky?		
...spending money got you or your family into trouble?		

If you checked YES to more than one of the above, have several of these ever happened during *at least a four day period of time*?

How much of a *problem* did any of these cause you -- like being unable to work; having family, money, or legal troubles; getting into arguments or fights?

No Problem   **Minor Problem**   **Moderate Problem**   **Serious Problem**

http://www.dbsalliance.org/pdfs/MDQ.pdf

Sensitivity and specificity of a new bipolar spectrum diagnostic scale.

* **OBJECTIVE:**

To assess the sensitivity and specificity of a self-report questionnaire for bipolar disorder, the Bipolar Spectrum Diagnostic Scale (BSDS).

* **METHODS:**

The BSDS was administered to 68 consecutive patients with bipolar illness and 27 consecutive patients with unipolar major depressive disorder. Created by Ronald Pies, it consists of a descriptive story that captures subtle features of bipolar illness, to which patients may assent on a sentence-by-sentence basis. BSDS scores were compared to clinicians' DSM-IV-based diagnoses.

* **RESULTS:**

Sensitivity of the BSDS was 0.76, approximately equal in bipolar I and II/NOS subjects (0.75 and 0.79, respectively). The BSDS identified 85% of unipolar-depressed patients as not having bipolar spectrum illness. A shift in the threshold of the BSDS resulted in a large increase in specificity (from 0.85 to 0.93), without a significant loss of sensitivity.

* **CONCLUSIONS:**

The BSDS was highly sensitive and specific for bipolar spectrum illness, especially with the amended threshold for positive diagnosis.

* http://www.psycheducation.org/PCP/launch/downloadMoodCheck.htm

bipolar spectrum diagnostic scale

MoodCheck

Part A. Please place a check after the statements below that *accurately describe you*.

During times when I am not using drugs or alcohol:	
I notice that my mood and/or energy levels shift drastically from time to time.	
At times, I am moody and/or energy level is very low, and at other times, and very high.	
During my "low" phases, I often feel a lack of energy, a need to stay in bed or get extra sleep, and little or no motivation to do things I need to do.	
I often put on weight during these periods.	
During my low phases, I often feel "blue," sad all the time, or depressed.	
Sometimes, during the low phases, I feel helpless or even suicidal.	
During the low phases, my ability to function at work or socially is impaired.	
Typically, the low phases last for a few weeks, but sometimes they last only a few days.	
I also experience a period of "normal" mood in between mood swings, during which my mood and energy level feels "right" and my ability to function is not disturbed.	
I then notice a marked shift or "switch" in the way I feel.	
My energy increases above what is normal for me, and I often get many things done I would not ordinarily be able to do.	
Sometimes during those "high" periods, I feel as if I have too much energy or feel "hyper".	
During these high periods, I may feel irritable, "on edge," or aggressive.	
During the high periods, I may take on too many activities at once.	
During the high periods, I may spend money in ways that cause me trouble.	
I may be more talkative, outgoing or sexual during these periods.	
Sometimes, my behavior during the high periods seems strange or annoying to others.	
Sometimes, I get into difficulty with co-workers or police during these high periods.	
Sometimes, I increase my alcohol or nonprescription drug use during the high periods.	
Total	

bipolar spectrum diagnostic scale

Part B. The statements in Part A (not just those checked) describe me (circle one of the answers below):

Not at all (0)	A little (2)	Fairly well (4)	Very well (6)

Add the number in parentheses in Part B to your checkmark total from Part A. _____

Part C.

Please indicate whether any of your (blood) relatives have had any of these concerns:					
	Grandparents	Parents	Aunts/Uncles	Brothers/Sisters	Children
Suicide	☐	☐	☐	☐	☐
Alcohol/Drug Problems	☐	☐	☐	☐	☐
Mental Hospital	☐	☐	☐	☐	☐
Depression Problems	☐	☐	☐	☐	☐
Manic or Bipolar	☐	☐	☐	☐	☐

	Yes	No
Has a health professional ever told you that you have manic-depressive illness or bipolar disorder?	Yes	No
Have you ever attempted suicide?	Yes	No

bipolar spectrum diagnostic scale

Part D.

How old were you when you first were depressed? *(circle one)*	As long as I can remember	Grade school	Middle school	High school	18-24	> 24
How many episodes of depression have you had?	One		2-4		5-6	>10
Have antidepressants ever caused: *(circle all that apply)*	Excessive energy	Severe insomnia	Agitation	Irritability	Racing thoughts	Talking a lot
How many antidepressants have you tried, if any?	None	1		2	3	>3
Has an antidepressant you took worked at first, then stopped working?	No			Yes		
Do your episodes *start* gradually, or suddenly?	Gradually		Can't say	Suddenly		
Do your episodes *stop* gradually, or suddenly?	Gradually		Can't say	Suddenly		
Did you have an episode after giving birth?	No		Within 6 months	Within 2 months		Within 2 weeks
Are your moods much different at different times of year?	No effect of time of year			Yes, seasonal shifts		
When you are depressed, do you sleep differently?	No		Sleep less		Sleep more	
When you are depressed, do you eat differently?	No		Eat less		Eat more	
When you are depressed, what happens to your energy?	Nothing	It varies a lot		Very low	Extremely low, can hardly move	
In episodes, have you lost contact with reality? (delusions, voices, people thought you were odd)	No			Yes		

If your total score from Parts A and B is **greater than 16**; or if you have **lots of circles** in shaded boxes on this page, you may need to learn more about "mood swings without mania". Use the Internet and search *Bipolar II* . This is something to learn about, not necessarily about *you*.

If your total score from Parts A and B is **less than 10**, and you have **few circles** in shaded boxes on this page, antidepressants are probably okay, if you and your doctor choose to use them. They can occasionally cause: unusual thoughts, including violent and suicidal ones; irritability; too much energy; and severe sleep problems. Contact your doctor if you think any of these might be happening to you.

The "Bipolarity Index"

* The system considers 5 "dimensions" of bipolarity. Note that the presence of hypomania or mania is only one of the five dimensions. All the others receive equal weight, for now (the system has not been subjected to the usual tests a "diagnostic instrument" would receive; thus we do not yet know how much weight each of these 5 dimensions should carry):

1. Hypomania or mania

2. Age of onset of first mood symptoms

3. Illness *course* and other features generally only visible *over time*

4. Response to medications (antidepressants and mood stabilizers)

5. Family history of mood and substance use problems

Dimension	20 points	15 points	10 points	5 points	2 points
Episode Characteristics	**Manic** symptoms with "prominent *euphoria*, grandiosity or expansiveness".	Manic symptoms with *dysphoria*, irritability	**Hypomanic** symptoms; or mania following an antidepressant	**Hypomanic** symptoms following an antidepressant; or hypomania below DSM threshold; or major **soft signs**: atypical or postpartum depression	Psychosis, without other signs of mania
Age of Onset	15-19	<15 or 20-30	30-45	>45	--
Illness Course (and Other Features)	Manic episodes separated by periods of full recovery	Incomplete recovery between manic episodes; or hypomania with full recovery between episodes	Mania, incomplete recovery, but also substance use; or psychosis only during mood episodes; or legal problems associated with mania	Repeated episodes of *unipolar* depression, no hypomania (3 or more); or hypomania with incomplete recovery between episodes; or any of several other features: borderline; anxiety disorder; ADHD as a child; gambling or other risk behaviors without mania per se; or PMS	Hyperthymic temperament; ≥3 marriages, or two jobs in two years; or two advanced degrees (see Akiskal reference on these latter features)
Response to Medications	Full **recovery** within *4 weeks* of treatment with mood stabilizers	Full **recovery** within *12 weeks* of treatment; or **relapse** within 12 weeks of stopping mood stabilizers; or **switch** to mania within 12 weeks of starting antidepressant	Worsening **dysphoria** or mixed state symptoms during antidepressant; or **partial response** to mood stabilizers; or antidepressant induced **rapid cycling** or worsening thereof	**Lack of response** to 3 or more antidepressants; or mania/hypomania when antidepressant *stopped*	**Immediate response**, almost complete, to antidepressant within 1 week or less
Family History	**1st degree relative** (brother/sister, parent, or child) with *clear bipolar* disorder	**2nd degree relative** with bipolar diagnosis; or 1st degree relative with recurring *unipolar* depression *and* features suggestive of bipolar disorder	**1st degree relative** with recurring *unipolar* depression or *schizoaffective* disorder; or **any relative** with *clear bipolar* diagnosis; or any other relative with unipolar depression and symptoms suggestive of bipolar	1st degree relative has clear problem with *drugs or alcohol*	1st degree relative has *repeated episodes of depression*; or has an anxiety disorder, an eating disorder, or ADHD

Dr. Sachs' article indicates that in their experience so far, most Bipolar **I** patients score above 60. Note that's Bipolar I, not Bipolar II or other more subtle variations, which would presumably have lower scores. Notice that a patient can "get points" for many different features of bipolarity, *not just hypomania or mania*. In fact, she could get 60 points even without any history of hypomania or mania at all, you see? For example, she might have had: her first depression at age 18 (20 points); post-partum depression (5 points); more than 3 episodes of depression (5 points); agitation while taking an antidepressant (10 points); and have a sister with clear bipolar disorder (20 points).   Acta Psychiatr Scand Suppl. 2004;(422):7-17. **Strategies for improving treatment of bipolar disorder: integration of measurement and management.** Sachs GS.

But beyond this -- Bipolar I patients score above 60 -- we do not yet know what a particular "score" might mean. Therefore this table is not offered to help you score patients (or yourself). It is presented to demonstrate that some of the most respected mood experts in the world are now using a system which approaches bipolar disorders as existing on a "spectrum", rather than a yes/no, you-have-it-or-you-don't matter. To see the Harvard version of this "Bipolarity Index", see page 13 of their Affective Disorders Evaluation.

Differential Diagnosis

* Major Depression:
  * Dysthymia, Bipolar depression, Cyclothymia, substance induced mood d/o, mood d/o due to GMC, Psychotic disorders, Adjustment disorders, Eating d/o, Anxiety d/o, Uncomplicated Bereavement
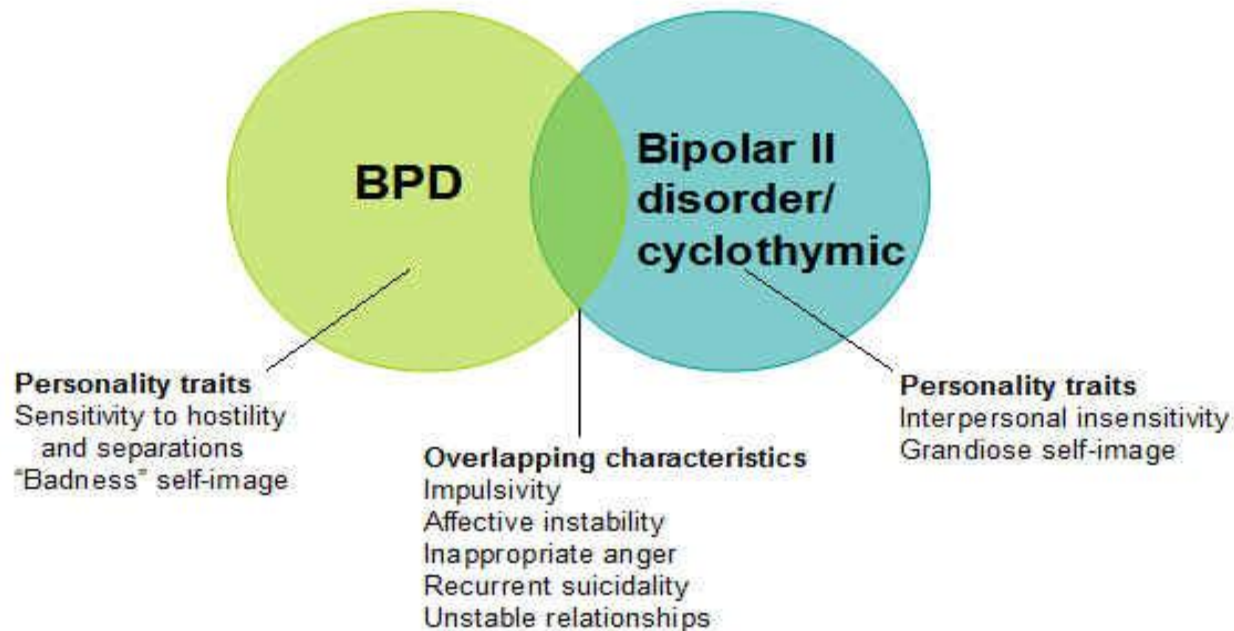* Bipolar D/O:
  * See above
  * manic episode : Bipolar I, II, Cyclothymia, GMC, Substance induced, PD (BPD, ASPD. Narcissistic, Histrionic PD) Schizophrenia
* Bipolar II:
  * Bipolar I , other mood d/o, BPD, Psychosis

Bipolar or Borderline?

Figure 2-3   Distinctions and overlapping characteristics between borderline personality disorder (BPD) and bipolar II disorder.

Distinguishing Bipolar from Borderline

Borderline PD (DSM list)	Bipolar (broad view)
Cognitive	*Cognitive*
unstable self	unstable self
transient paranoid ideation	psychosis, esp. paranoid/grandiose
chronic emptiness	_____
abandonment fear	_____
Energy	*Energy*
impulsivity	impulsivity
(sex, substances, self-harm)	(spending, sex, substances, risk sports)
Mood	*Mood*
affective instability	affective instability
reactive mood	"rejection hypersensitivity"
episodic dysphoria	dysphoria
irritability, intense anger	irritability, intense anger
anxiety	anxiety
Behavior	*Behavior*
suicide attempts (~10%)	suicide attempts (~10%)
self-harm	self-harm?

Other Organic Diagnoses

* It is important to first rule out the possibility of any other organic diagnosis:
  * Thyroid disorder
  * Seizure disorder
  * Multiple sclerosis
  * Infectious, toxic, and drug-induced disorders
    * Steroids
    * Beta agonists
    * Synthroid
    * Parkinson's meds
    * Stimulants
    * Hallucinogens

Epidemiology of Bipolar Disorder

* Prevalence: Bipolar I:1% of population Adults = Adolescents
* Bipolar Spectrum: around 4%
* Males = Females Bipolar I
* Males < Females Bipolar II
* 2-3 million American adults are diagnosed with bipolar disorder
* NIMH estimates that one in very one hundred people will develop the disorder

Course

* long course, multiple relapses
* Life stressors precede most often the first episode vs. subsequent ones
* MDD:
  * untreated mood episode lasts 6-13 months,
  * treated 1 to 3months
* Bipolar d/o:
  * Untreated episode lasts a mean of 13 weeks
  * 75% recover within 1 year
  * mean age onset 32, about 6-10 years after first depressive episode
  * Only 10-20% experience only manic episodes
  * Treatment reduces risk of relapse and number of episodes by 50%

PROGNOSIS

* MDD: chronic illness, relapses –
    * 25% relapse within 6months after hospitalization
    * 30-50% relapse within first 2 years after hosp
    * 50-75% relapse within first 5years
* Bipolar do: poorer then MDD
    * 40-50% can have second mood episode within 2 years
        * 7% bipolar I do not have recurrence
        * 45% >1episode
        * 40% chronic d/o
    * Mean # manic episodes 9 (2-30)
    * Long term f/u – 15% are well; 45% well but relapses; 30% partial remission; 10% chronic
* Bipolar II: chronic illness
* 15% life time completed suicide (Bipolar I = Bipolar II)

Therapy

* Mood Stabilizers
* Lithium
* Divalproex Sodium (Depakote)
* Carbamezapine
* Atypical Antipsychotics
* ECT/TMS
* Psychotherapy
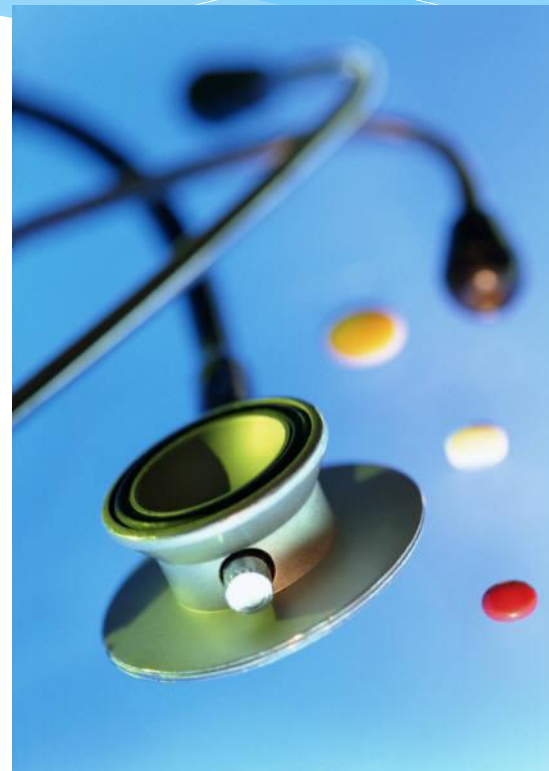
Lithium Carbonate

Eskalith Lithobid

* Salt of a monovalent ion -?blocks Inositol Phosphatases
* 900-1800 mg/day level= 0.6 to 1.2 mEq/L
* FDA-labeled Indications: Bipolar disorder, manic episode and maintenance therapy
* Monitoring : CBC, CHEM, TSH, Pregnancy, ECG baseline – level q3mo, renal/TSH q3mo then q6mo
* Common SE: ECG changes, GI (N/V) , muscle weakness, polyuria, EEG changes, tremor, hyperreflexia, sedation
* Serious SE: arrhythmia, hypotension, ataxia, coma, Sz, tinnnitus, polyuria
* Lithium toxicity: >1.5mEq/L – tremor, Nausea, Diarrhea, blurry vision, dizziness, confusion, tinnitus, increased DTR; >2.5mEq/L – Sz, Coma, Arrhythmias

Valproic Acid <u>DEPAKENE Divalproex Sodium   DEPAKOTE</u>

* GABA Re activation
* 750-3600mg –for plasma level, 50-125 mcg/mL;
* Monitoring: CBC, LFT, level q3mo
* FDA –Labeled Indications: Manic Bipolar I, Sz do
* Non-FDA: Bipolar I /II Maintenance, Schizoaffective do – bipolar type, ETOH WD
* Black Box Warning – hepatotoxic, teratogenic
* Common SE– sedation ,GI, elev. LFT, Tremor, Osteoporosis, Thrombocytopenia, alopecia, weight gain
* **Serious :** Tachycardia , Hyperammonemia , Pancreatitis , Thrombocytopenia, Dose-related , Liver failure , Ototoxicity
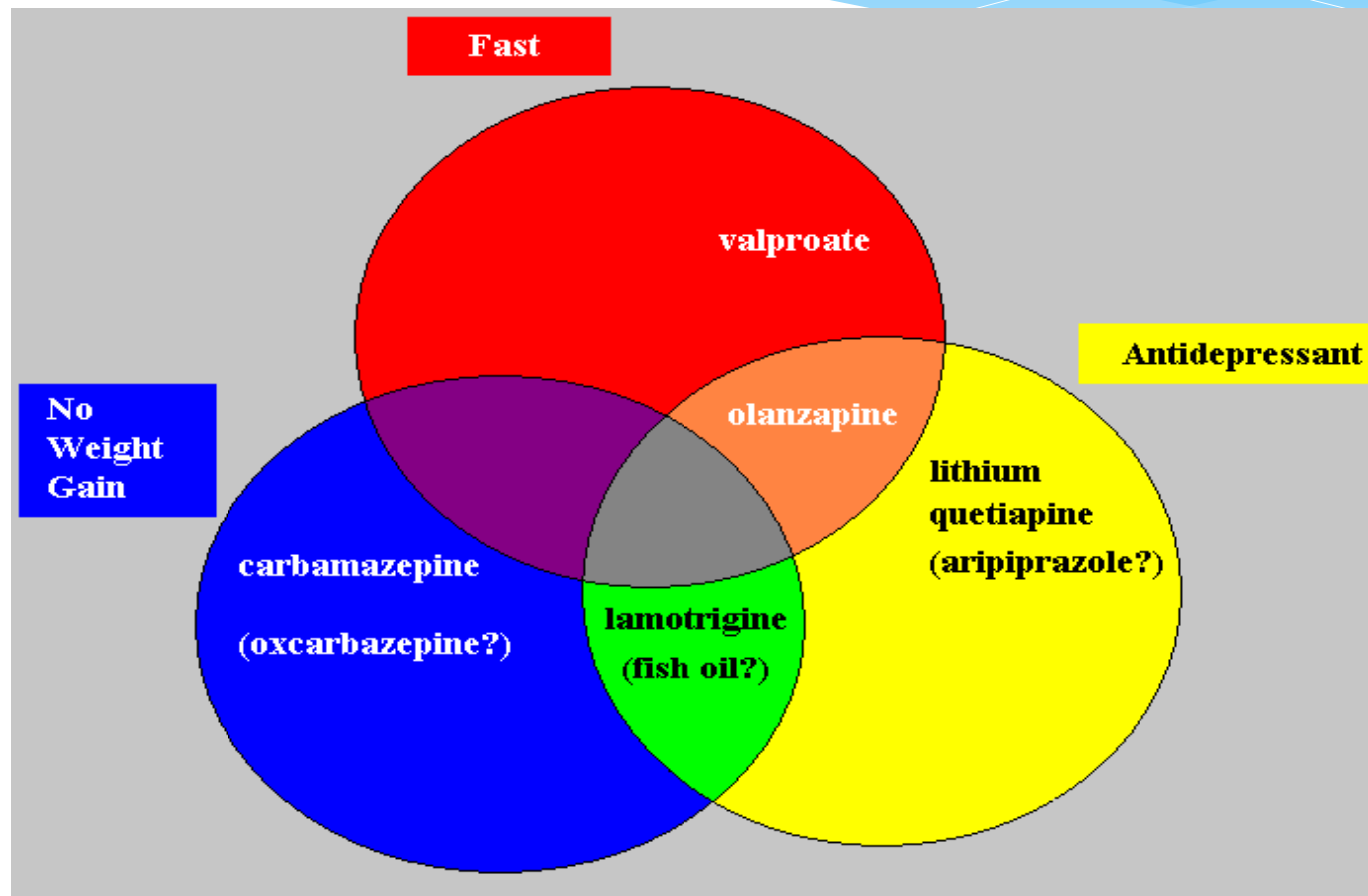* Toxicity: -sedation, heart block, Coma

CARBAMAZEPINE:
Tegretol

* Related structurally to TCA , reduces the polysynaptic response
* 200mg BID to 1600mg /day – for 4-12µg/ml
* FDA : Bipolar I disorder, acute manic and mixed episodes, Epilepsy, Trigeminal neuralgia
* NonFDA : Agitation (TBI, Dementia, MR), RLS, Cocaine Dep, ETOH/BZD WD
* Black Box: skin, agranulocytosis, aplastic anemia
* **Common SE :** Hyper/Hypotension, N/V, Confusion, Dizziness, Nystagmus, Sedation, Blurred vision, Diplopia
* **Toxicity -** dizzy, ataxia, sedation, diplopia, nystagmus, ophthalmoplegia, Cerebellar sx, EPS, Sz, respiratory failure, Tachycardia, hypotension, Arrhythmias, irritability, stupor, coma

Lamotrigene
LaMICTAL

* blocks voltage-sensitive sodium channels ,
* 25 mg/day ORALLY for 2 weeks, then 50 mg/day for 2 weeks, then 100 mg/day for 1 week, then 200 mg/day; max 400mg/day
* FDA Labeled indication: **Bipolar 1 disorder**
* Non-FDA :Bipolar disorder, depressed phase, Tx resistant Depression
* **Black Box Warning: rash**
* **Common SE: r**ash , Indigestion , N/V, Asthenia Pain , Ataxia, Dizziness , HA, Somnolence , Blurred vision , Diplopia , Anxiety
* **Serious:** Erythema multiforme , Stevens-Johnson syndrome, Toxic epidermal necrolysis Anemia, Disseminated intravascular coagulation, Eosinophil count raised, Leukopenia, Thrombocytopenia , Liver failure , Amnesia , Seizure , Angioedema
* If with Depakote – need to decrease Lamotrigene dose by 50% due to drug drug interaction.

Mood Stabilizers

Randomized trials positive	Randomized trials *negative*	Open trials suggestive	Case reports/series	For Bipolar Depression
lithium (Lithobid, Eskalith)	gabapentin (Neurontin)	zonisamide (Zonegran)	thyroid hormone (T3/T4)	(not "mood stabilizers": *no anti-manic effects*)
valproate, divalproex (Depakote)	topiramate (Topomax)	clozapine	High-dose thyroid hormone	Dopamine agonists pramipexole, ropinirole
carbamazepine (Carbatrol, Tegretol)	tiagabine (Gabatril)	levitiracetam as an antimanic (not as an antidepressant)	memantine	Light therapy for bipolar depression
lamotrigine (Lamictal)			E.M. Power Plus (a.k.a. TrueHope) (40 vitamins/minerals)	n-acetylcysteine
olanzapine (Zyprexa) *quetiapine* (Seroquel) lurasidone (Latuda)			acetazolamide ketogenic diet	celecoxib? (very preliminary but very interesting) modafinil
(verapamil)	(verapamil)		phenytoin (Dilantin) (N= 23, controlled)	High-dose thyroid hormone
omega-3 fatty acids (fish oil)			transcranial magnetic stimulation (TMS)	not levetiracetam?
oxcarbazepine (Trileptal) *risperidone* (Risperdal) *aripiprazole* (the trade name is just too smarmy, sorry; it has to go in small print: Abilify) ziprasidone (Geodon)				

BIPOLAR DISORDER Treatment

* **DEPRESSED EPISODE:**

  * First line: Lithium or Lamotrigene
    * OK: Lithium + antidepressant (CI antidepressant alone)

  * Severe sx or pregnant: ECT

  * Refractory:
    * Add Lamotrigene,
    * Add Wellbutrin /Paxil, other SSRI, SNRI, MAOI
    * ECT

BIPOLAR DISORDER Treatment

* **MANIC EPISODE:**
  * MODERATE: Lithium or Valproic Acid or Olanzapine
  * SEVERE: Lithium or Valproic Acid AND Olanzapine or Risperidone AND/OR BZD for agitation
* **MIXED or SA Hx :**
  * VPA better than Lithium
* **BREAKTHROUGH :** increase dose, add NL or BZD
* **RAPID CYCLING (>4 mood episodes/year):** Carbamazepine
* **REFRACTORY:**
  * ADD first line (Lithium+Depakote)
  * ADD Carbamazepine or Oxcarbazepine
  * ADD NL or Change NL (Clozaril)
  * ECT – if refractory mania or mixed or pregnant

Atypical Antipsychotics

* Clozapine (Clozaril)
* Risperidone (Risperdal)
* Olanzapine (Zyprexa)
* Quetiapine (Seroquel)
* Aripiprazole (Abilify)
* Ziprasidone (Geodon)
* Lurasidone (Latuda)
* Asenapine (Saphris)
* Iloperidone (Fanapt)
* Paliperidone (Invega)

Atypical Antipsychotics (ctd.)

* Uniformly used for acute **M**ania because they can cause rapid patient stabilization.
* Few approved as multipurpose mood stabilizers (quetiapine, olanzapine, lurasidone)
* Exhibit a "class-effect" on mania unlike anticonvulsants though not all FDA approved.
* All require lipid panels and FBS for monitoring though only clozapine, olanzapine, risperidone and quetiapine are most likely to cause changes.

In late 2013, a group of bipolar disorder specialists from the International Society for Bipolar Disorders published their recommendations in one of the top psychiatric journals.
Am J Psychiatry. 2013 Nov 1;170(11):1249-62. doi: 10.1176/appi.ajp.2013.13020185

Acute treatment	**1. Adjunctive antidepressants may be used for an acute bipolar I or II depressive episode when there is a history of previous positive response to antidepressants.**
	2. Adjunctive antidepressants should be avoided for an acute bipolar I or II depressive episode with two or more concomitant core manic symptoms in the presence of psychomotor agitation or rapid cycling.
Maintenance treatment	**3. Maintenance treatment with adjunctive antidepressants may be considered if a patient relapses into a depressive episode after stopping antidepressant therapy.**
Monotherapy	**4. Antidepressant monotherapy should be avoided in bipolar I disorder.**
	5. Antidepressant monotherapy should be avoided in bipolar I and II depression with two or more concomitant core manic symptoms.
Switch to mania, hypomania, or mixed states and rapid cycling	**6. Bipolar patients starting antidepressants should be closely monitored for signs of hypomania or mania and increased psychomotor agitation, in which case antidepressants should be discontinued.**
	7. The use of antidepressants should be discouraged if there is a history of past mania, hypomania, or mixed episodes emerging during antidepressant treatment.
	8. Antidepressant use should be avoided in bipolar patients with a high mood instability (i.e., a high number of episodes) or with a history of rapid cycling.
Use in mixed states	**9. Antidepressants should be avoided during manic and depressive episodes with mixed features.**
	10. Antidepressants should be avoided in bipolar patients with predominantly mixed states.
	11. Previously prescribed antidepressants should be discontinued in patients currently experiencing mixed states.
Drug class	**12. Adjunctive treatment with norepinephrine-serotonin reuptake inhibitors or tri- and tetracyclics should be considered only after other antidepressants have been tried, and should be closely monitored because of an increased risk of mood switch or destabilization.**

The Bottom Line on using Antidepressants

Acute	1. *Okay* if previous positive response
	2. Avoid if ≥ 2 manic symptoms
	3. Avoid in mixed states.
	4. Avoid if history of predominantly mixed states
	5. Avoid if history of rapid cycling
	6. Avoid if previously *induced* hypomania/mania or mixed states
Maintenance	7. *Okay* if relapse after stopping
Monotherapy	8. Avoid in Bipolar I
Induced mixed, rapid cycling, hypomania/mania	9. Stop (monitor closely for…)
Drug type	10. Avoid SNRI or TCA

MaintenanceTreatment

* **MAINTENANCE:** >6months
  * Lithium or VPA
  * Lamotrigene, Carbamazepine, Oxcarbazepine
  * ECT
  * D/C antipsychotic if no ongoing psychotic sx
  * Atypicals are increasingly used if regular relapse
* High relapse rate
* Geller longitudinal study
  * 1 year recovery rate 37%
  * 1 year relapse rate   38%

Is Bipolar under or over-diagnosed?

* Phelps J. *Bipolar disorder: particle or wave? DSM categories or spectrum dimensions?* Psychiatric Times. 2006. http://www.psychiatrictimes.com/bipolar-disorder/content/article/10168/46826. Accessed January 3, 2012. 3.
* Roan S. *Bipolar disorder may be over-diagnosed.* Los Angeles Times. 2008. http://latimesblogs.latimes.com/booster_shots/2008/05/bipolar-disorde.html. Accessed January 3, 2012.4.
* Zimmerman M, Ruggero CJ, Chelminski I, Young D. *Is bipolar disorder overdiagnosed?* J Clin Psychiatry. 2008;69:935-940.5.
* Angst J, Azorin JM, Bowden CL, et al. *Prevalence and characteristics of undiagnosed bipolar disorders in patients with a major depressive episode: the BRIDGE study.* Arch Gen Psychiatry. 2011;68:791-798.6.
* Parker G, Graham R, Hadzi-Pavlovic D, et al. *Does testing for bimodality clarify whether the bipolar disorders are categorically or dimensionally different to unipolar depressive disorders?* J Affect Disord. 2011 Oct 24. [Epub ahead of print].
* Sobo, Simon **Mood Stabilizers and Mood Swings: In Search of a Definition** Psychiatric Times, October 01, 1999

* See more at: http://www.psychiatrictimes.com/bipolar-disorder/update-bipolar-disorder-particle-or-wave#sthash.lfjV65WP.dpuf

Why the Problem?
(Decision-making and behavioral biases)

* <u>Confirmation bias</u> — the tendency to search for or interpret information in a way that confirms one's preconceptions.
* <u>Congruence bias</u> — the tendency to test hypotheses exclusively through direct testing, in contrast to tests of possible alternative hypotheses.
* <u>Framing</u> - drawing different conclusions from the same information, depending on how that information is presented.
* <u>Information bias</u> — the tendency to seek information even when it cannot affect action.
* <u>Selective perception</u> — the tendency for expectations to affect perception.
* <u>Reactance</u> - the urge to do the opposite of what someone wants you to do out of a need to resist a perceived attempt to constrain your freedom of choice.
* <u>Anchoring</u> — the tendency to rely too heavily, or "anchor," on a past reference or on one trait or piece of information when making decisions.
* <u>Clustering illusion</u> — the tendency to see patterns where actually none exist.

Memory biases impacting history taking

* Beneffectance - perceiving oneself as responsible for desirable outcomes but not responsible for undesirable ones. (Term coined by Greenwald (1980))
* Consistency bias- incorrectly remembering one's past attitudes and behaviour as resembling present attitudes and behaviour.
* Cryptomnesia - a form of misattribution where a memory is mistaken for imagination.
* Egocentric bias - recalling the past in a self-serving manner, e.g. remembering one's exam grades as being better than they were, or remembering a caught fish as being bigger than it was
* Confabulation or false memory - Remembering something that never actually happened.
* Hindsight bias - filtering memory of past events through present knowledge, so that those events look more predictable than they actually were; also known as the 'I-knew-it-all-along effect'.
* Selective Memory and selective reporting
* Suggestibility - a form of misattribution where ideas suggested by a questioner are mistaken for memory. Often a key aspect of hypnotherapy.
* Obsequiousness bias - the tendency to systematically alter responses in the direction they perceive desired by the investigator.
* Impact bias — the tendency for people to overestimate the length or the intensity of the impact of future feeling states.

Social Biases

* <u>Actor-observer bias</u> — the tendency for explanations for other individual's behaviors to overemphasize the influence of their personality and underemphasize the influence of their situation. This is coupled with the opposite tendency for the self in that one's explanations for their own behaviors overemphasize their situation and underemphasize the influence of their personality. (see also fundamental attribution error).

* <u>Fundamental attribution error</u> — the tendency for people to over-emphasize personality-based explanations for behaviors observed in others while under-emphasizing the role and power of situational influences on the same behavior (see also actor-observer bias, group attribution error, positivity effect, and negativity effect).

* <u>Bandwagon effect</u> — the tendency to do (or believe) things because many other people do (or believe) the same. Related to group think, crowd psychology, herd behaviour, and manias.

o <u>Self-fulfilling prophecy</u> — the tendency to engage in behaviors that elicit results which will (consciously or subconsciously) confirm our beliefs.

o Kahneman, Daniel; <u>Thinking, Fast and Slow;</u> Farrar, Straus and Giroux, New York