## Bipolar Disorder for Project ECHO

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#### The Spectrum

Every time I have taught students about bipolar illness, I have always deeply offended someone. I have recently realized that is because I usually see very ill people.

At its worse, bipolar disease is an extremely disabling condition that starts to merge with schizophrenia, with manic episodes that produce the very grandiose delusional experiences that every medical student remembers from his/ her psychiatric rotation.

But many people with Bipolar illness have bipolar 2 disorder or cyclothymia, which usually means long periods of severe depression only infrequently punctuated with "hypomania" for a week or so.

Many people with (and without) personality disorders have been told that they have bipolar illness and certainly cannot relate to the psychotic experiences of some full-blown manic episodes and will tell you that they have been told that they are bipolar because their moods go "up and down" within minutes to hours,





### Defining a few terms that will be useful

#### Manic Episode:

 A distinct period of abnormally and persistently elevated, expansive, or irritable mood AND persistently increased goal-directed activity lasting at least a week, most of the day, nearly every day (or so bad person needs to be hospitalized)

#### Hypomanic Episode:

 A distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased activity or energy, lasting at least 4 consecutive days, present most of the day, and nearly every day. By definition it CANNOT cause marked impairment and the patient cannot have psychosis.

#### A Major Depressive Episode:

• Having either a depressed mood or a loss of interest or pleasure + changes in sleep, appetite, low energy, feelings of guilt, poor concentration and/ or suicidal ideation for the same 2 week period.





### Mixed Episodes:

#### Hypomanic or Manic Episode with mixed features:

- Full criteria are met for manic or hypomanic episode + 3 or more of the following:
  - Prominent dysphoria or depressed mood
  - Diminished pleasure and interest in all or almost all activities
  - Psychomotor retardation
  - Fatigue/ loss of energy
  - Feelings of worthlessness or excessive guilt.
  - Recurrent thoughts about death or suicide.





### Making the Correct Diagnosis

Bipolar 1 Disorder: If a patient has every had a full manic episode EVER, then he, by definition has Bipolar 1 disorder. If the patient is currently depressed, then the diagnosis is Bipolar 1 disorder, currently depressed (NOT major depressive disorder)!!

Bipolar 2 disorder: If a patient has ever had a hypomanic episode AND has also met full criteria for a major depressive episode, he has Bipolar 2 disorder. If he is currently depressed, the correct diagnosis is Bipolar 2 Disorder, currently depressed.

Cyclothymic: If a patient has a lot of ups and downs, but NONE of them meet criteria for Mania, Hypomania, of Major depression, he has cyclothymic.





## What if the patient's situation doesn't really match any of those criteria exactly?

Then use the "other specified" or "unspecified category."

#### Use this for:

- Hypomanic episode that are not long enough.
- A hypomanic episode without evidence of a proceeding Major Depressive Episode
- Cyclothymic that lasts less than 24 months.
- A manic episode that only happened when a person took an antidepressant.





# What if there are drugs involved of the patient has a medical illness that seemed to have caused the episodes?

#### Drugs known to cause Mania:

- PCP: delirium and then mania within hours to a few days
- Stimulants (cocaine, meth, Ritalin): Symptoms within minutes to hours, usually resolves in a couple of days at the most.
- Corticosteroids cause mania or a mixed state several days after ingestion: higher doses much more likely to cause problems.
- If caused by an antidepressant, DO NOT USE this designation.

#### MEDICAL conditions associated with mania.

- Stroke or Traumatic Brain Injury or Frontotemporal Dementia
- Cushing's disease (too much Cortisol)
- Multiple Sclerosis
- Hyperthyroid conditions.





#### Case #1

• A 41-year-old patient is brought in with his family. He has not been sleeping. He believes he is able to communicate with animals, has propositioned strangers for sex, got into a bar fight and is spending large amounts of money. He attempted to purify the children by spraying then with Pine Sol® and crushed Fruit Loops® into the carpet of his front room. Family reports that he got mugged by wandering around at night and was held at knife point when he taunted the mugger. He says that he feels "fantastic." Patient reports that strippers had assaulted him sexually, he is the "literal reincarnation" of Apollo, and that his assets are worth "millions and millions of dollars." He corners your medical student of Middle Eastern descent and explains that he should reject ISIS and go by the name "Zander" because "we all love the same God." Before this episode, the patient worked as an accountant and was well liked and respected in his community.







#### A quick note about Counter-Transference

People who are in a manic phase of a bipolar illness are often Grandiose. In the presence of a grandiose person, one can feel:

- Annoyed
- Belittled
- -Intruded upon
- Castigated

This should give you the information that you are in the presence of a manic individual who is not at his/ her baseline. If this is the person's baseline, think about a personality disorder (especially narcissism).







## For Bipolar 1 Disorder you only need one episode of MANIA defined as below:

A distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting at least 1 week (or any duration if hospitalization is necessary).

During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree.

- 1. inflated self-esteem or grandiosity
- 2. decreased need for sleep (e.g., feels rested after only 3 hours of sleep)
- 3. more talkative than usual or pressure to keep talking
- 4. flight of ideas or subjective experience that thoughts are racing
- 5. distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli)
- 6. increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
- 7. excessive involvement in pleasurable activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)





### Or more memorably...

DIG FAST for at least 1 week, 3 or 4 symptoms.

**D** = Distractibility and easy frustration

I = Irresponsibility and erratic uninhibited behavior

**G** = Grandiosity

**F** = Flight of ideas

A = Activity increased with weight loss and increased libido

**S** = Sleep is decreased

**T** = Talkativeness





A manic episode lasts at least 1 week, most days of the week, most of each day. (shorter if a person is so sick they need to be hospitalized).

I feel better than average (mania).

Euthymic Baseline: I feel "fine"

Lets say this line is about a year long.

Bipolar 1 Disorder: All you need to be diagnosed with Bipolar 1 disorder is one period meeting criteria for a manic episodes one time in your life.

Most people with Bipolar 1 Disorder also have periods of depression, but this is not a necessary element for the diagnosis.

I feel worse than average (depression).





## Interesting Tidbits about Bipolar 1 disorder

12 month prevalence 0.6%

M>F 1.1:1

Mean age of onset of first mood episode (manic, hypomanic, depressed) is 18, but onset as a child or as a 70 year old is relatively common.

90% of people with a manic episode with have future mood episodes. For 60% of people, a depressed episode comes right after the manic one.

Very genetic: 10X risk if close family member has the illness. Shares risk genes with schizophrenia.

Females are more likely to have rapid cycling or mixed states and spend more time in depression compared to males. Males have higher rates of comorbid substance use disorders

Suicide risk is at least 15X higher than general population

Even between episodes, 30% of patient struggle socially or occupationally and are more likely to have cognitive impairments.

Many with bipolar 1 also have anxiety disorders, half meet criteria for alcohol use disorder. Treatment can cause Metabolic problems.





### Psychosis?

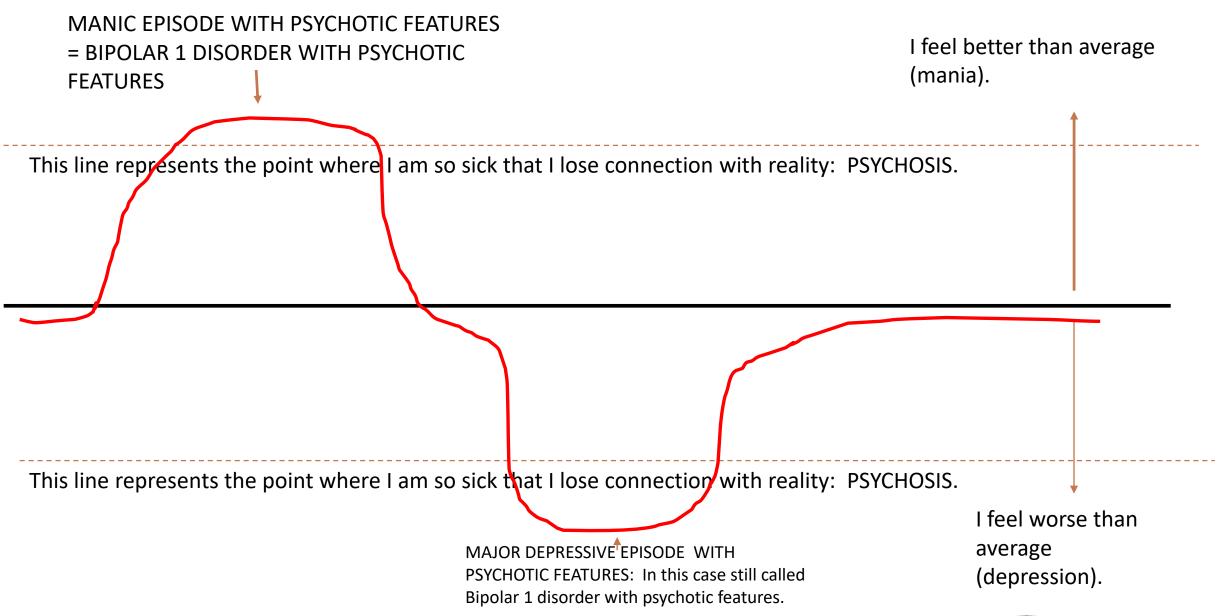
Psychosis means "fundamentally losing touch with reality."

Psychosis can be a feature of stresses or normal life (being very tired, dehydrated), Severe Medical illness (delirium), or practically any psychiatric illness (OCD, Depression, or mania)

People with severe bipolar disorder frequently lose touch with reality. If they do lose touch with reality, it cannot be Bipolar 2 disorder (hypomania) anymore.











## Manic People Frequently need to be Hospitalized.

Danger to Self (walking outside naked in January/ picking fights with the Hell's Angels).

Danger to Others (impulsive, reckless driving).

Gross inability to care for their own needs.





#### Case #2



Maria is an accomplished comedian who presents with complaints of depression. She has very low energy, spends all day in bed, very little facial movement on the interview. On history she reports periods in the past which have lasted up to a week where she has needed very little sleep, has had racing thoughts, and increased goal directed activity, but she has never been admitted to a hospital or lost touch with reality or gotten into too much trouble: but these periods have certainly strained her relationships.





### Bipolar 2 Disorder (EL Dos)

Period of mood disturbance and increased energy and activity, with 3 or 4 of the following symptoms, representing a NOTICABLE CHANGE from BASELINE

- Inflated self-esteem or grandiosity
- Decreased need for sleep
- More talkative or pressure to keep talking
- Flight of ideas or feeling of thoughts racing.
- Distractibility
- Increase in goal directed activity (socially, at school, work or sexually)
- Excessive involvement in activities with high potential for painful consequences.

Must be noticeable by others, but NOT be severe enough to cause social/occupational dysfunction or result in Hospitalization.

Patient has to have a history of a Major Depressive Episode meeting full criteria.

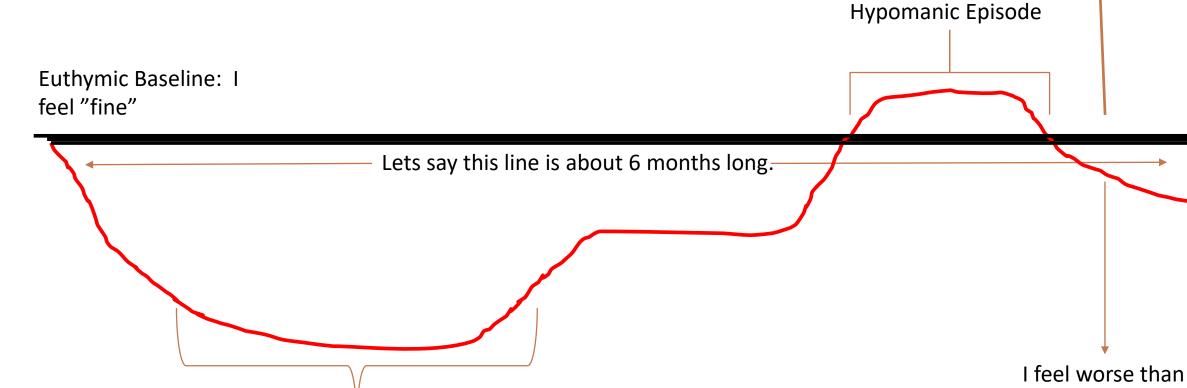




For Bipolar 2 Disorder you must have at least one episode meeting full criteria for <u>Major Depression</u> AND one episode of <u>Hypomania</u> over a lifetime.

Major Depressive Episode

I feel better than average (mania).





average

(depression).



### What is wrong with a little Hypomania?

Usually nothing, the problem is usually the severe, difficult to treat depression that follows the hypomanic episode.

Most of the time the patient comes with depression and you need to dig to get the hypomanic symptoms (or get information from a family member/ friend) of the patient.





#### **Tidbits**

12 month prevalence in USA 0.8%, in other countries average is 0.3%

Average age of onset is the mid-20s.

M=F

12% of people with a major depressive episode will go on to develop/ be diagnosed with bipolar 2 disorder

~15% are rapid cyclers (higher rate than for bipolar 1). Rapid cycling = worse prognosis

~15% will go on to eventually get Bipolar 1 diagnosis.

Genetically, more related to family members with Bipolar 2, than Bipolar 1

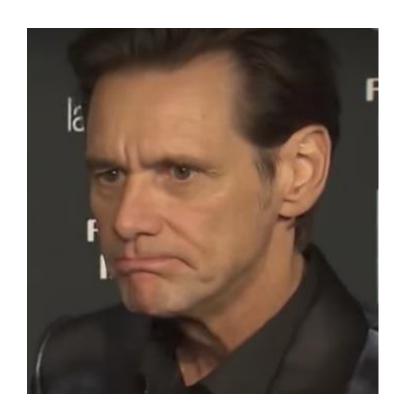
Suicide attempts is similar to people with bipolar 1 disorder, but Bipolar 2 patients more likely to complete.

75% have comorbid Anxiety, 37% have substance use disorder, 14% have had an eating disorder at some time in the past.





#### Case #3



Jim is a 50 year old man who presents for mood changes and depression. For the last 2-3 years he feels like his mood changes from week to week or month to month. Some months he has a ton of energy, great ideas, and works really hard. Other months he feels tired and drained and unhappy. His mood changes are straining his marriage. He has never been hospitalized. Never had a suicide attempt.





### Cyclothymic Disorder

At least 2 years with numerous periods of hypo-hypomania and numerous episodes of depressive symptoms that don't meet criteria for Major Depressive Episode.

The symptoms have been present for at least half of the 2 year period and the patient is not without symptoms for more than 2 months at a time

Criteria for major depressive, manic, or hypomanic episodes have never been met.

Symptoms cause clinically significant impairment or distress





Cyclothymia: Over at least two years, multiple mood episodes. **None of them** meeting criteria for Mania, Major Depressive, or Hypomania. These symptoms must cause clinically significant distress or impairment.

I feel better than average (mania).

Euthymic Baseline: I feel "fine"

Lets say this line is about 6 months long.

I feel worse than average (depression).





### **Tidbits**

12 month prevalence 0.4-1.0%

M=F, but females present more frequently for treatment.

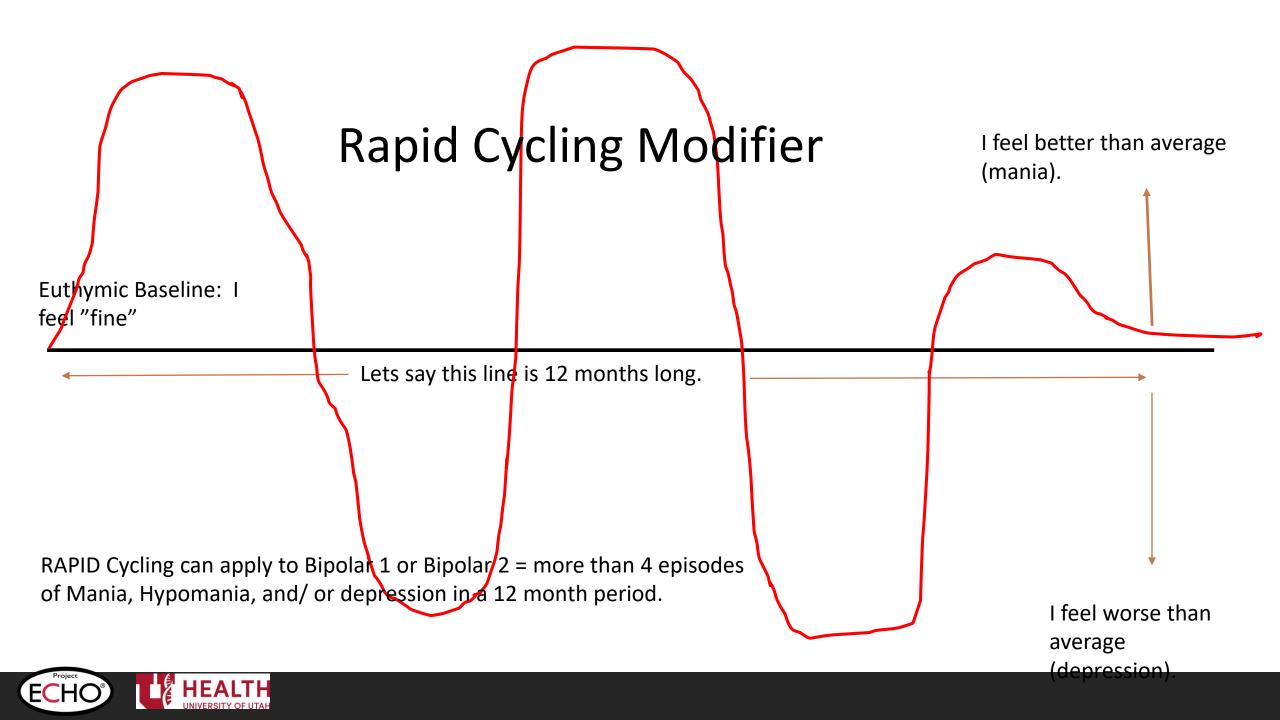
Starts in late adolescence/ early adulthood

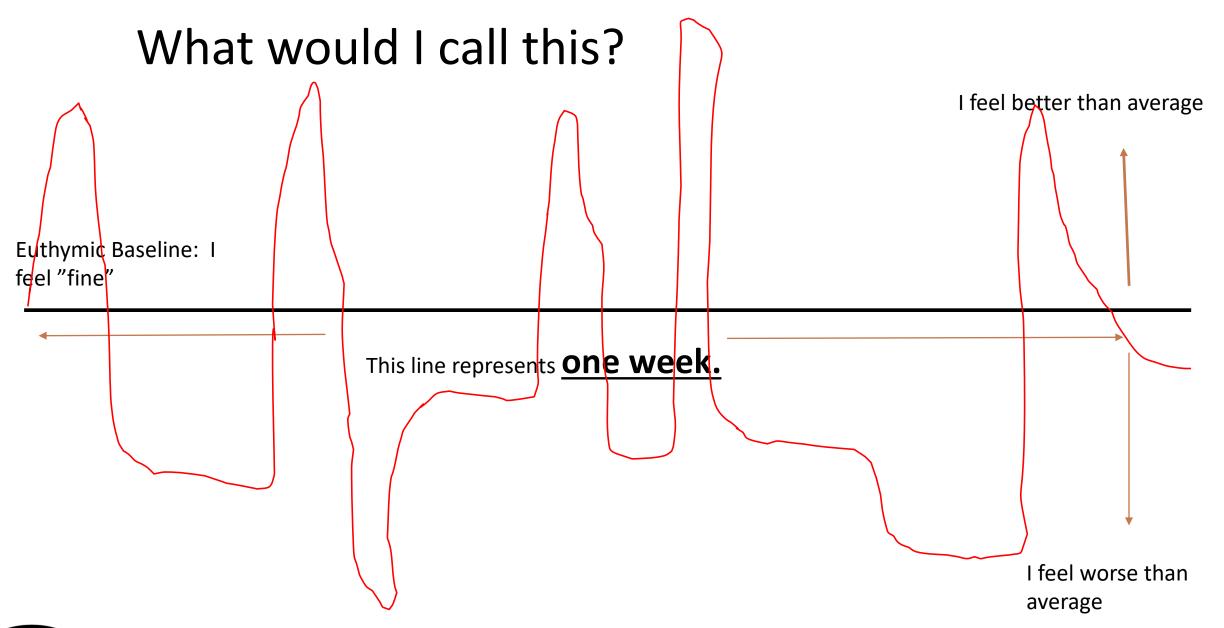
15-50% go on to be diagnosed with bipolar 1 or 2

More likely to have relatives with bipolar 1, bipolar 2, or major Depressive Disorder.













## Affective Instability is NOT the same as a Bipolar Mood Disorder

In order for someone to have mania, hypomania, or Major Depression, the episode has to last at least 4-7 days.

Many people who do NOT have Bipolar Disorder will tell you that their moods go up and down "one minute I am really happy, then next I am sad/ angry/ irritable"

This is called Affective Instability and is actually one of the most sensitive measures of Borderline Personality Disorder

Please don't tell people who have borderline personality disorder that they have Bipolar Disorder, mostly because it keeps them from getting psychotherapeutic help that will be the most helpful for their conditions.

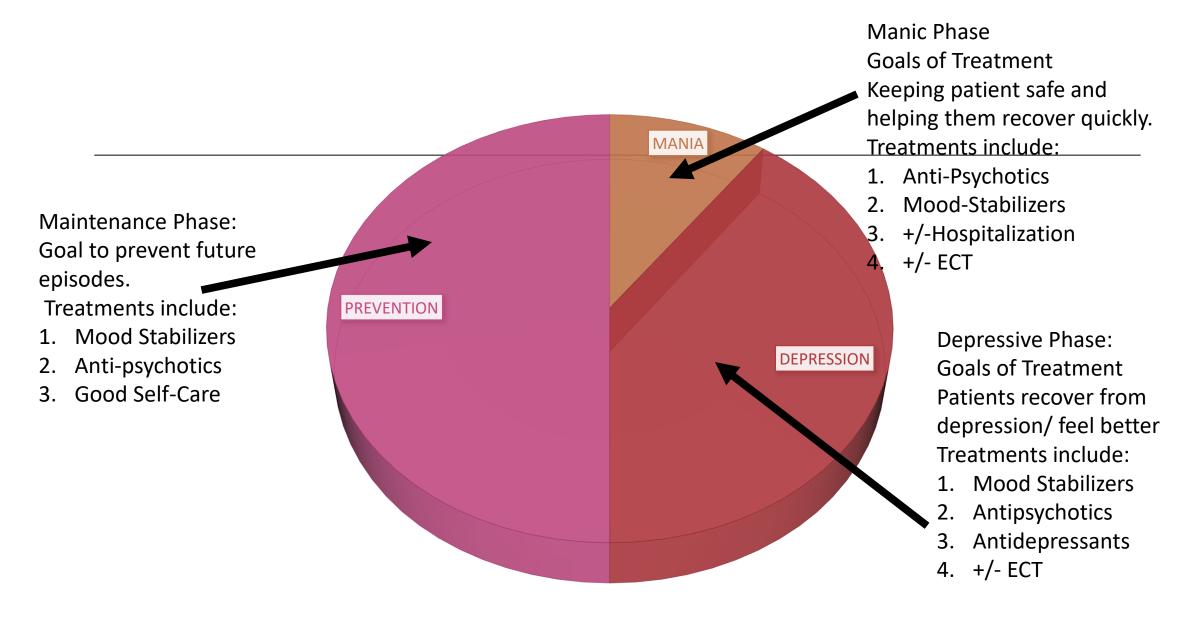




## A very brief graphic on treatment.











## Manic People Frequently need to be Hospitalized.

- Danger to Self (walking outside naked in January/ picking fights with the Hell's Angels).
- Danger to Others (impulsive, reckless driving).
- Gross inability to care for their own needs.





## Manic Individuals are usually treated with an Antipsychotic and a Mood-Stabilizer.

- All Antipsychotic stop dopamine transmission in the brain.
  - The first antipsychotic, Chlopromazine (Thorazine®) was released in the 1950's led to the miraculous recovery of many people who had been very ill for years.
  - **Mood Stabilizers** include Lithium (the 3<sup>rd</sup> element on the periodic table) and almost any drug that was designed to treat seizures, though Valproic Acid (Depakote®) and Carbamazepine (Tegretol®) are used most frequently.





#### FDA Approved Treatments for Bipolar Mania

- Mood Stabilizers:
  - Lithium
  - Valproic Acid
  - Carbamazepine (Extended-Release)
- Antipsychotics
  - Chlopromazine (Thorazine®)
  - Olanzapine (Zyprexa ®)
  - Quetiapine (Seroquel<sup>®</sup>)
  - Risperidone (Risperdal<sup>®</sup>)
  - Ziprasidone (Geodon®)
  - Aripiprazole (Abilify®)
  - Cariprazine (Vraylar®)
  - Asenapine (Saphris ®)
- New antipsychotics not (yet) approved for bipolar mania
  - Brexpiprazole (Rexulti®)
  - Iloperidone (Fanapt®)
  - Paliperidone (Invega®)
  - Lurasidone (Latuda®)





#### Lithium

#### Good Things:

- All Natural (3<sup>rd</sup> element on the periodic table). Some natural springs have Lithium and have helped people for centuries. Used to be ingredient in 7-UP.
- Has robust evidence in treating Bipolar disorder, but also reducing suicidality/ self-harm behaviors and lowering risk of dementia associated with bipolar disorder.

#### Bad Things:

- Narrow therapeutic window. Can easily become toxic in circumstances of dehydration or with almost anything that messes with kidneys (NSAIDS, Thiaizides, ACE-I, ARBS)
- Over time will frequently cause hypothyroidism and nephrogenic DI.
- Patients who are unlikely to be compliant can actually be worse off from starting and then stopping this medication.
- Doesn't work as quickly in acute mania as other agents.





#### Valproic Acid/ Carbamazepine

#### Good Things:

- Works quickly
- Relatively forgiving therapeutic window
- Stops seizures

#### Bad Things:

- Bad for anyone who could become pregnant. Avoid in women of childbearing age (especially if they are impulsive, which many bipolar people are).
- Hair loss and weight gain and PCOS are common with Valproic Acid
- Rare badness includes for Valproic Acid includes liver dysfunction (elevated LFTS, elevated ammonia) and rate cases of life threatening pancreatitis. For Carbamazepine: hyponatremia (really low sodium levels) and low blood counts (especially platelets) are common.





## Antipsychotics: Usually necessary for the acutely manic hospitalized patient and work quickly, but have drawbacks.....

- Because they all block dopamine, antipsychotics can increase risk for drugrelated neurological conditions: dystonias, akathisia, and tardive dyskinesia
- Many increase Prolactin and therefore interfere with reproductive function leading to sexual dysfunction/ milk discharge/ male-breast development.
- Many can contribute to heart arrhythmias by prolonging the QT interval.
- Newer antipsychotics also hit various other receptors besides dopamine (Serotonin / Histamine/ and others) and therefore have a unique set of slightly different benefits and drawbacks.
- For newer antipsychotics (especially our most effective ones), massive weight gain, diabetes, and cholesterol derangements are major problems.





#### Antipsychotic Delivery Techniques

- Most medications must be taken as a pill.
- Some can be given as an **intramuscular injection** (IM) for a patient who is agitated.
- Some dissolve with saliva before being swallowed as a way to get around patients who may spit out the pills.
- Some dissolve and the medicine is absorbed through the cheek.
- Some medications can be given once every 2-8 weeks in a Long Acting Injection (LAI).
- A new medication is even available to be inhaled.





#### Bipolar Depression

- Regular antidepressants are usually a poor choice in bipolar depression, but can be helpful for some patients.
- 4 medications are FDA approved for Bipolar Depression:
  - Quetiapine (Seroquel®)
  - Olanzapine/ Fluoxetine combination (Symbyax®)
  - Lurasidone (Latuda®)
  - Cariprazine (Vraylar®)
- Medications that are NOT FDA approved, but have some evidence:
  - Lamotrigine (Lamictal®)
  - Lithium
  - SSRIs





## Bipolar Maintenance: Keeping people from getting sick.

- Currently approved medications are:
  - Aripiprazole (Abilify®)
  - Lamotrigine (Lamictal®)
  - Lithium
  - Olanzapine (Zyprexa®)
  - Quetiapine (Seroquel®)
  - Risperidone LAI (Risperdone Consta®)
  - Ziprasidone (Geodon®)



