TREATMENT OF BIPOLAR DISORDER IN THE PRIMARY CARE SETTING

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Disclosures

- None

Learning Objectives

1. Understand epidemiology of bipolar disorder in the general population and in primary care practice.
2. Understand new DSM criteria for bipolar disorder.
3. Understand how to diagnose bipolar disorder in the primary care setting.
4. Understand safety assessment in the primary care setting.
5. Understand evidence-based treatments for the various phases of bipolar disorder and be able to implement these treatments in the primary care setting.
6. Understand when the use of antipsychotic medication is indicated.
7. Understand the assessment and treatment of common comorbidities of bipolar disorder in the primary care setting.
8. Understand when patients should be referred to a psychiatrist.

Outline

- Disclosures
- Learning Objectives
- Why Discuss This Topic?
- Epidemiology
- How to Equip a Practice to Treat Patients with Bipolar Disorder
- Diagnosis and Treatment
  - Various phases of bipolar disorder
  - 4 Cases
- Managing Side Effects
- Long-term monitoring
- When to Refer to Psychiatry
- Celebrities with Bipolar Disorder
- References

Why Discuss This Topic?
Case 1 - Brad

- ID: 18 year old male high school senior from Madison, Maine brought to his PCP by his mother.
- CC: "I've been feeling wicked depressed."
- HPI:
  - 3 week history of:
    - Depressed mood
    - Poor sleep
    - Increased energy
    - Anhedonia
    - Problems concentrating
    - Decreased appetite
    - Intermittent suicidal ideation without plan or intent
- PMHx: None
- FamHx: Mom has poorly treated Bipolar II disorder

Why Discuss This Topic?
Case 1 - Brad

- Further discussion reveals…
  - Reports having racing thoughts
  - Talking faster than usual
  - Appears to be very irritable
  - Episodes of anger and rage
    - Recently destroyed his room and frightened his mom
      - Very out of character
  - Increased sex drive recently
    - Looking at porn online
      - Out of character
  - Speeding ticket
    - Driving 70 mph on a back road in Central Maine
      - Out of character

Why Discuss This Topic?
Case 1 - Brad

- PCP diagnosed him with “depression”
- Given prescription for fluoxetine (Prozac)
  - Did not sleep for 6 nights
  - Began experiencing auditory and visual hallucinations
  - Began feeling paranoid
  - Irritability, depression and suicidal ideation worsened

Why Discuss This Topic?
Case 1 - Brad

- Returned to PCP
- Mom mentioned possible diagnosis of bipolar disorder.
- PCP said “I’m not comfortable treating that”
  - Prozac discontinued and trazodone started
  - Referred to Acadia Hospital for psychiatric evaluation
  - Family unable to follow up at Acadia
    - Brad’s family’s limited health insurance will not pay for treatment at Acadia
    - Acadia is far from home

Brad is currently not receiving any mental health treatment!

Bipolar Disorder - Statistics

- Lifetime prevalence = 4% of U.S. population
- More common in high-income countries
- Large genetic component
  - 10-fold increased risk among adult relatives
- High risk for suicide
  - Suicide risk = at least 15 times that of the general population
  - Accounts for ¼ of all completed suicides

http://www.nimh.nih.gov/statistics/

Bipolar Disorder - Impact

- Bipolar disorder can lead to:
  - Decreased quality of life and functional status
  - Lost of employment
  - Difficulty regaining employment
  - Days lost from work
  - Increase interactions with criminal justice system
- Significant Medical Comorbidity
  - Increased comorbid substance use disorders
  - Diabetes mellitus, hepatitis C, low back pain, and pulmonary conditions are more common in patients with bipolar disorder than non-bipolar patients

www.nami.org

Kilbourne AM et al. *Burden of general medical conditions among individuals with bipolar disorder.* **Bipolar Disorders.** 2004. 6:5, 368-373.

Bipolar Disorder - Impact

- Most expensive mental health care diagnosis
- 6th leading cause of disability worldwide.
- 1991 prevalence-based cost-of-illness study
  - Total annual costs were estimated at $45.2 billion

www.nami.org
Centers for Disease Control
Kilbourne AM et al. *Burden of general medical conditions among individuals with bipolar disorder.* **Bipolar Disorders.** 2004. 6:5, 368-373.

Bipolar Disorder - Impact

- For every $1 spent on outpatient care for patients with bipolar disorder, $1.80 is spent on inpatient care.
- Only 18.8% of patients with the disorder are getting minimally adequate treatment

81.2% of Bipolar patients are NOT receiving minimally adequate treatment!

National Institute of Mental Health
Centers for Disease Control

Can Bipolar Disorder be successfully treated in a primary care clinic?

YES!

Steps to Treating Bipolar Disorder in Primary Care Practice

1. Prepare the Practice
2. Diagnose Bipolar Disorder
3. Provide Psychiatric Treatment
4. Provide Medical Treatment
5. Provide Support

Culpepper L. *The Role of Primary Care Clinicians in Diagnosing and Treating Bipolar Disorder*. **Prim Care Companion J Clin Psychiatry.** 2010; 12(Suppl 1): 4–9.

Step #1: Prepare the Practice

1. Define level of management to be assumed by practice
   - Each patient will need short-term and long-term treatment goals
   - Ultimate goal = recovery
   - Acute vs. maintenance treatment
2. Train staff
   - How to manage disruptive patients
3. Set up systems for follow-up and monitoring
   - Practice bipolar registry system
4. Contact referral and support services for safety concerns, complex cases, and pharmacologic expertise
5. Develop crisis response strategies
6. Prepare Web resources
   - National Alliance for Mentally Ill (NAMI)
   - National Institute for Mental Health (NIMH)

Culpepper L. *The Role of Primary care Clinicians in Diagnosing and Treating Bipolar Disorder*. **Prim Care Companion J Clin Psychiatry.** 2010; 12(Suppl 1): 4–9.

Steps to Treating Bipolar Disorder in Primary Care Practice

1. Prepare the Practice
2. **Diagnose Bipolar Disorder**
3. **Provide Psychiatric Treatment**
   - For Bipolar Disorder AND for comorbidities
4. **Provide Medical Treatment**
   - Monitor for and treat side effects
   - Check for comorbidities
5. Provide Support

Culpepper L. *The Role of Primary Care Clinicians in Diagnosing and Treating Bipolar Disorder*. **Prim Care Companion J Clin Psychiatry.** 2010; 12(Suppl 1): 4–9.

Step #5 - Provide support

- Monitor for medication adherence
  - Provide/prescribe pill reminder boxes
  - Check serum levels
- Instruct in self-monitoring and response to prodromal symptoms
  - Mood charts
- Provide support through transitions
- Improve problem-solving skills
- Treat medication side effects

Diagnosing, Treating, and Monitoring Bipolar Disorder

Diagnosis- Key Issue

Whenever ANYONE presents with a chief complaint of “depression”, you MUST screen for bipolar disorder.

Treatment for unipolar depression is VERY different from treatment from bipolar disorder.

Treatment- Key Features

- There are different evidence-based treatments available for the different phases of the disorder
- Ideally want something to treat both hypo/manic and depressed phases of the disorder
  - Example:
    - If the patient is currently depressed but has a history of mania, it is ideal to prescribe something that will treat BOTH the current depression and the future mania (instead of one medication for depression and another medication for mania)
- Aim for monotherapy
  - Multiple medications are frequently needed

Phases of Bipolar Disorder – Key Points

- New DSM-V Criteria for Bipolar I and Bipolar II Disorders
- Phase of the disorder is VERY important - Treatment varies with the phase of the disorder!
- Most common phase = DEPRESSED PHASE
- Remember:
  - A young adult with depression, no history of mania/hypomania may actually have bipolar disorder and simply not yet experienced mania/hypomania

Phases of Bipolar Disorder

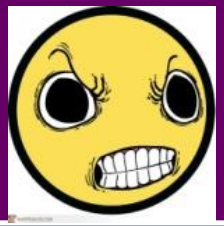
Major Depressive Episode

Hypomanic Episode

Manic Episode

Manic/hypomanic Episode with Mixed Features

Depressed Episode with Mixed Features



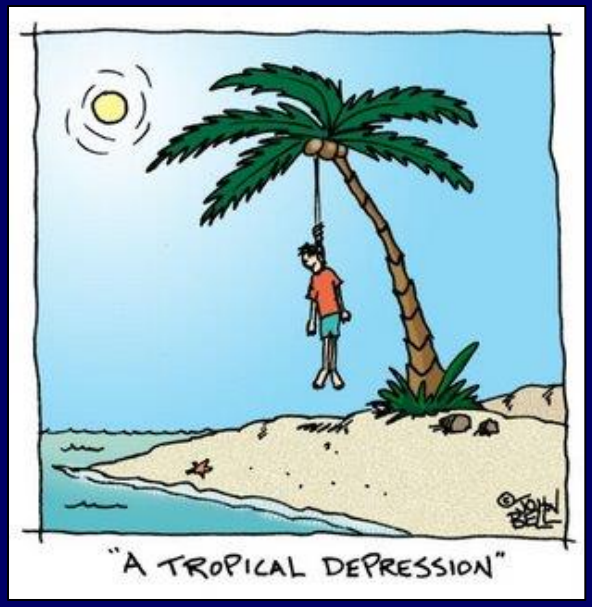
Treatment varies with the phase of the disorder!

Simplified DSM-V Criteria for Major Depressive Episode

Either depressed mood OR loss of interest or pleasure

AND 5 + of the following symptoms

1. Anhedonia
2. Weight loss/gain or decrease/increase in appetite
3. Insomnia or hypersomnia
4. Psychomotor agitation or retardation nearly every day
5. Fatigue or loss of energy
6. Feelings of worthlessness or guilt
7. Problems with concentration
8. Suicide
   - Recurrent thoughts of death
   - Recurrent suicidal ideation without a specific plan
   - Suicide attempt
   - Specific plan for committing suicide.



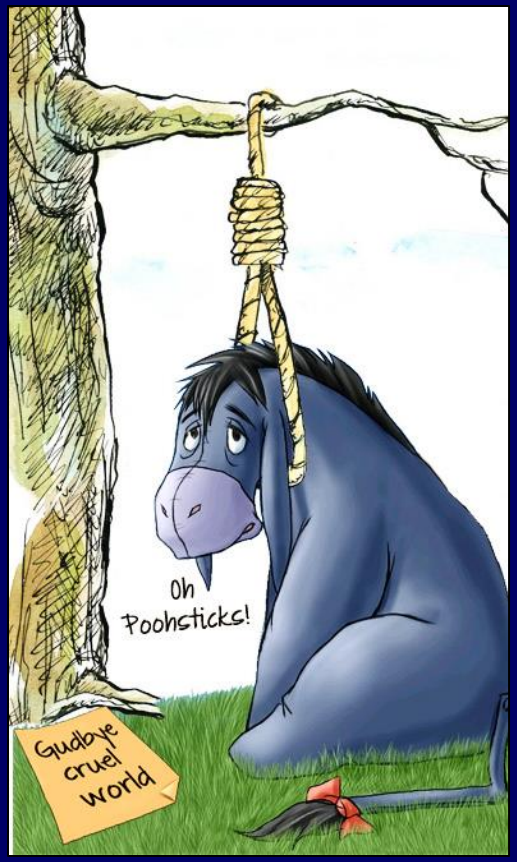
Simplified DSM-V Criteria for Major Depressive Episode

- **S** Sleep
- **I** Interest
- **G** Guilt
- **E** Energy
- **C** Concentration
- **A** Appetite
- **P** Psychomotor
- **S** Suicide

Be sure to ask about psychosis.
(Are you hearing voices? Do you think people want to harm you? Etc.)

Depression- Safety

- Primary care physicians assess for suicide in patients with depression in only about 1/3 of visits.
- 50% of persons who commit suicide had sought professional help in prior month
- Assess suicide risk
  - Ask: “This past week, have you had any thoughts that life is not worth living or that you’d be better off dead?”
  - Ideation, intent, plan, availability, lethality



Feldman et al. *Do Patient Requests for Antidepressants Enhance or Hinder Physicians' Evaluation of Depression?: A Randomized Controlled Trial.* 2006. **Medical Care;** 44(12):1107-1113.

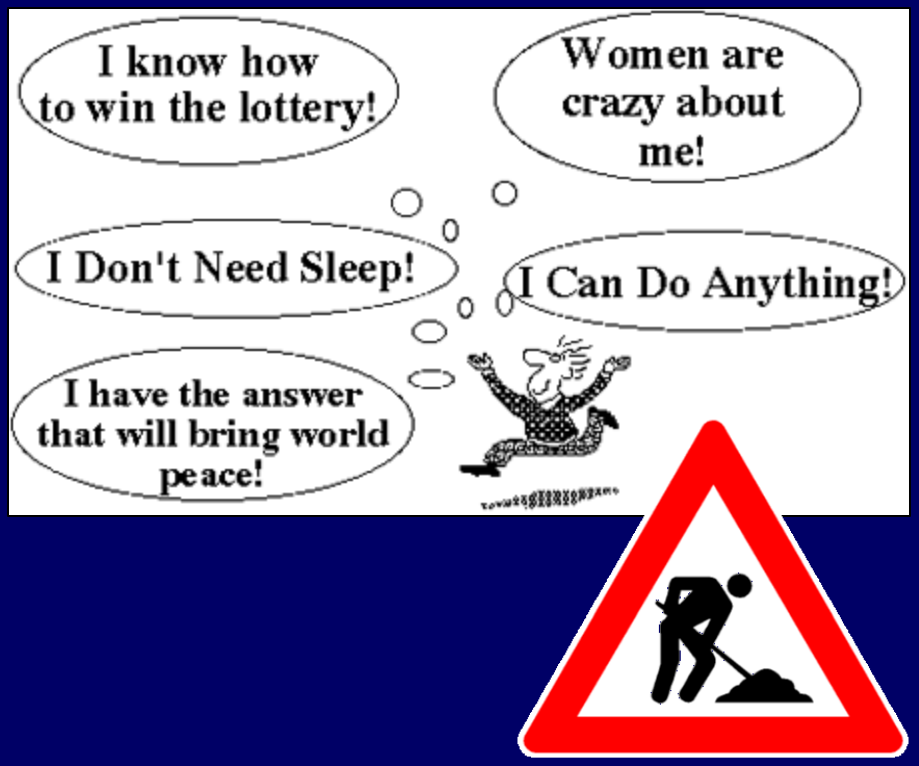
Simplified DSM-V Criteria for Hypomanic and Manic Episodes

- Abnormally elevated, expansive, or irritable mood AND increased activity / energy
- PLUS Need 3 + of the following (4+ if mood is only irritable):
  - Inflated self-esteem
  - Decreased need for sleep
  - More talkative than usual or pressure to keep talking.
  - Flight of ideas or racing thoughts.
  - Distractibility
  - Activities that have a high potential for painful consequences.
    - Gambling, prostitution, maxing out credit cards, driving very fast, etc.

www.offthemark.com
www.acuteaday.com

Simplified DSM-V Criteria for Hypomanic and Manic Episodes

- **D** Distractibility
- **I** Indiscretion
- **G** Grandiosity
- **F** Flight of Ideas
- **A** Activity Increase
- **S** Sleep Deficit
- **T** Talkativeness



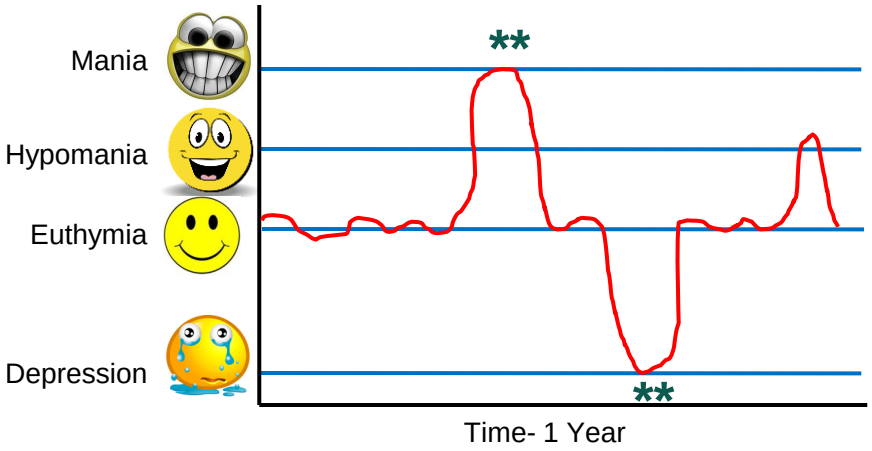
D, G, F, A, and T can usually be observed.
Be sure to ask about psychosis.
(Are you hearing voices? Do you think people want to harm you? Etc.)

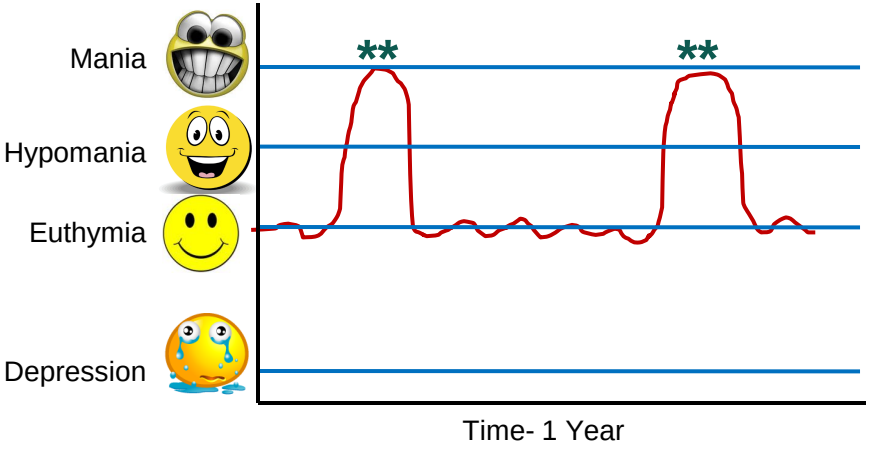
Mania versus Hypomania

- Mania
  - Bipolar I Disorder only
  - 7 consecutive days
    - Any duration if hospitalization is needed
  - Psychosis may be present
  - Severe functional impairment
  - Recommend hospitalization for these patients unless you are comfortable providing adequate outpatient treatment
  - Not suicidal BUT may be a danger to themselves due to poor self care and/or poor judgment

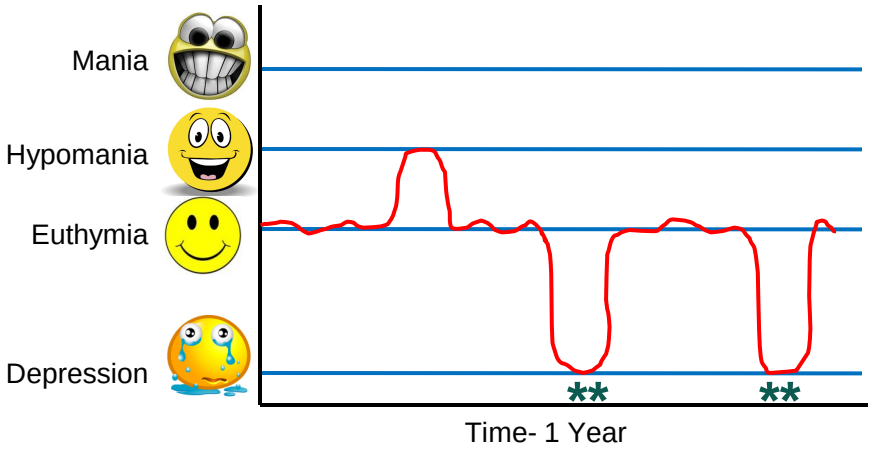
- Hypomania
  - Present in both Bipolar I and Bipolar II Disorders.
  - 4 consecutive days
  - NO psychosis (in Bipolar II psychosis is only seen during depression)
  - **NOT** severe enough to cause marked impairment in social/occupational functioning or to require hospitalization.

BIPOLAR I





BIPOLAR II



** Psychosis may be present

Case 2 - Katie

- ID: 25 yo female who is new to your practice
- CC: "I've been really depressed for the past month"
- HPI:
  - Depressed mood
  - Increased sleep
  - Low energy
  - Anhedonia
  - Problems concentrating
  - 10 lb weight gain
  - Feelings of worthlessness
  - Denies suicidal ideation
- PMHx:
  - Asthma
  - Previous Diagnosis of "Depression"
- FamHx:
  - Father with Bipolar I Disorder
  - Sister with Bipolar II Disorder
  - Son with ADHD

www.theguardian.com

Case 2 - Katie

- Further discussion
  - Denies any history of mania/hypomania
  - Previously tried:
    - venlafaxine (Effexor)
      - Caused irritability and insomnia
    - escitalopram (Lexapro)
      - Ineffective

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Case 2 - Katie

- If unsure whether or not a patient has bipolar depression or unipolar depression:
  - If you/the patient would prefer to try an antidepressant before moving to a mood stabilizer…
    - Best choice is bupropion
      - No serotonin action
      - Least likely to cause irritability or switch to mania
    - 2nd choice- SSRI (not fluoxetine due to long half-life)
    - Worst Choices:
      - Tricyclic antidepressants
      - Venlafaxine and other drugs with NE action

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Case 2a - Katie

- ID: 25 yo female returns to your practice 6 weeks later and she brings her husband
- CC: "The depression is worse, the bupropion didn't help, and I remembered something…"
- Additional Info:
  - Hypomanic episode several months ago prior to the depression.
  - She didn't realize it was hypomania until after she discussed it with her husband.
  - During the 6 day episode:
    - Mood was "awesome"
    - Thoughts were racing and her husband said she "talked way to fast"
    - Maxed out her Visa card on "stupid stuff" (her husband was displeased!)
    - Slept only 2 hours per night- wasn't tired, spent time frantically cleaning the house, waking her husband and son.
    - Spent hours online playing "slot machine games" and lost several hundred dollars.

Treatment- Bipolar Depressive Episode

1. Stop Antidepressants
   - Antidepressants can **worsen** depression in bipolar disorder
2. Lithium (Lithobid, etc.)
3. Quetiapine (Quetiapine)

Can treat both depression AND hypomania/mania

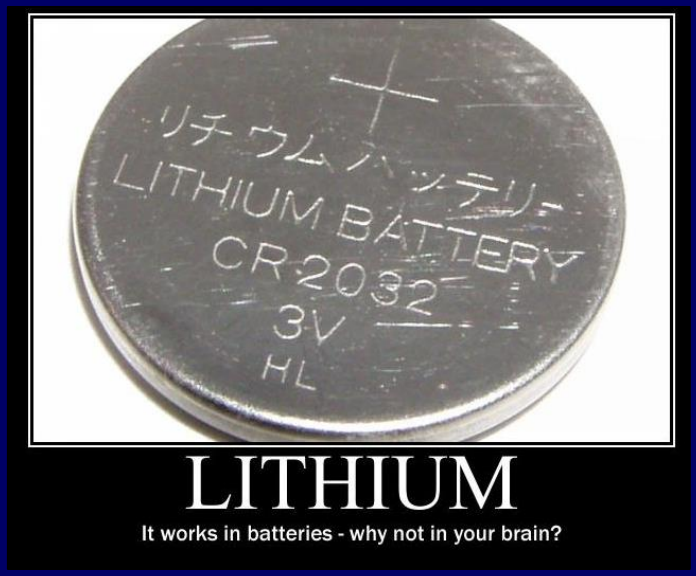
4. Lamotrigine (Lamictal)
5. Lurasidone (Latuda)
6. Refer to Psychiatry

Remember- when choosing a treatment, aim for monotherapy and a medication that can treat multiple phases of the disorder

Ansari A & Osser D. *The Psychopharmacology Algorithm Project at the Harvard South Shore Program: An Update on Bipolar Depression.* 2010. **Harv Rev Psychiatry.** 36-55.

Lithium

- FDA-approved for mania but not depression (no financial incentive)
- **Best evidence-based treatment for both manic and depressed phases of bipolar disorder**
- Generally well-tolerated
- Inexpensive
- Neuroprotective
- Anti-suicide effect (Clozapine is the only other medication with this effect)
- More complicated to prescribe than other medications but WORTH THE EFFORT



Lithium

- Baseline labs
  - CBC, renal function, TSH, EKG, pregnancy test
- Check other medications
  - Furosemide, Thiazides, ACEI can increase lithium levels
  - NSAIDS can increase lithium levels
- Key side effects
  - Renal toxicity
  - Thyrotoxicity
  - Acne
  - Benign leukocytosis
  - GI side effects
  - Some weight gain
  - Polyuria/polydypsia
  - Headache
  - Tremor

Lithium

- How to prescribe:
  - **Short-acting formulation** is best for kidneys and works as well as long-acting formulation
  - Single dose at bedtime to decrease daytime side effects
- Dose:
  - Start at 150-300mg qHS
  - Have patient follow-up in 1 week to check a lithium level, assess for tolerability, ask about suicidality again, etc.
  - Increase dose every week until an effective dose is reached based on level. Meet with patient weekly until a proper dose is achieved.
- Levels:
  - Obtain trough levels- 12 hours after last dose
  - Acute depression or mania
    - Level of 0.8-1.1
  - Maintenance of depression
    - Level of 0.6-0.75
  - Maintenance of mania
    - Level of 0.8-1.0

Prescribing lithium-
More effort in the beginning, but less work and fewer issues long-term.

Lithium

- Toxicity
  - Symptoms
    - Lethargy
    - Weakness
    - Confusion
    - Nausea, vomiting, diarrhea
    - Tremor
    - Ataxia
    - Possible seizures or coma
- Treatment
  - Stop lithium and monitor levels
  - Gastric lavage in cases of recent overdose
  - IV Fluids
  - Dialysis

Lithium

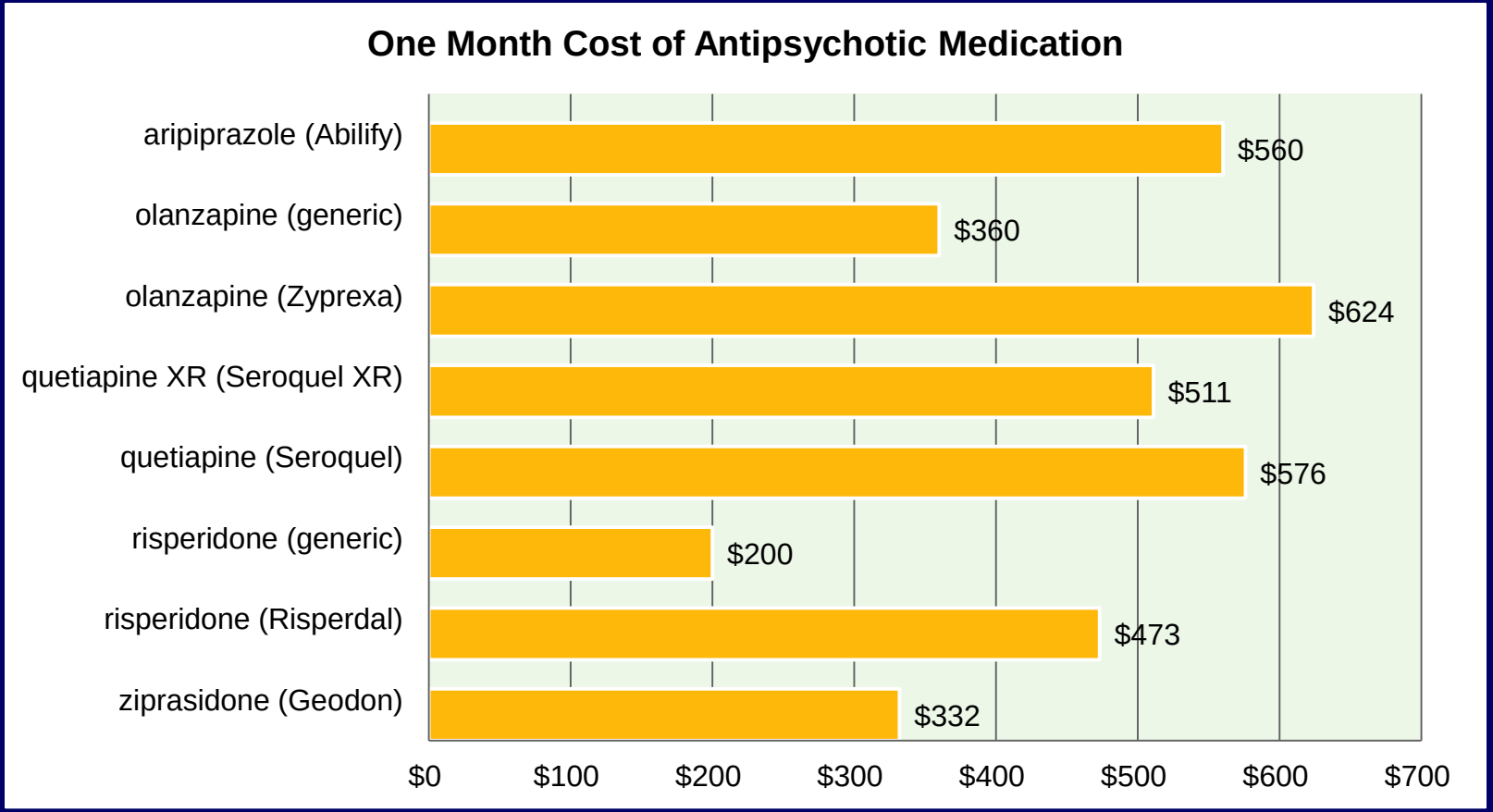
- Managing Side Effects
  - Hypothyroidism
    - Monitor TSH and treat with levothyroxine
  - GI side effects
    - Usually resolve on their own
  - Polyuria/polydypsia
    - Treatments:
      - HCTZ paradoxical effect
        - Monitor K+ levels and lithium level
      - Amiloride
        - Monitor lithium level
  - Tremor
    - Treat with propranolol

Monitoring Patients Taking Lithium

- Check a serum lithium level ~ 7 days after every dose change
  - You must wait 7 days after a dose change due to the half-life of lithium
- Be sure to check trough levels
- Once stable, check lithium level, TSH, renal function at least twice every year.

Why Start with Lithium and NOT an Antipsychotic?

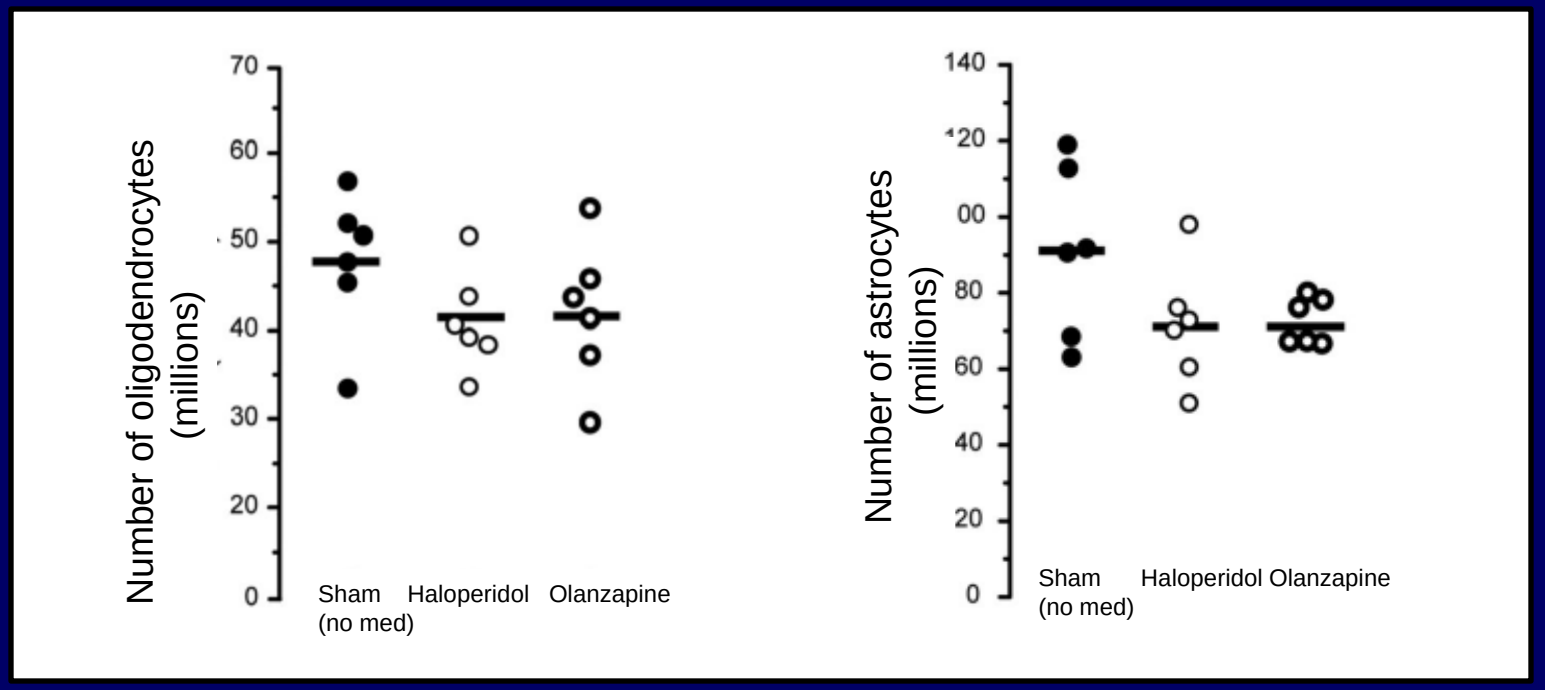
- Antipsychotics are not always indicated (hypomania, mania or depression without psychotic features)
- Cost



Modified from Scheurer D. et al. *Restrained Use of Antipsychotic Medications: Rational Management of Irrationality*. 2012. **Independent Drug Information Service**.

Why Start with Lithium and NOT an Antipsychotic?

Decreased gray matter volume due to antipsychotic use



Konopaske GT, Dorph-Petersen KA, *Sweet RA, et al. Effect of chronic antipsychotic exposure on astrocyte and oligodendrocyte numbers in macaque monkeys.* 2008. **Biol Psychiatry**; 63:759-65

Antipsychotics Side Effects

- Muscarinic acetylcholine receptor anti-cholinergic effects
  - Dry mouth and skin
  - Blurry vision
  - Tachycardia
  - Sedation
  - Constipation
  - Urinary retention
  - Angle closure glaucoma
- Alpha-1 adrenergic receptor effects
  - Orthostatic hypotension
  - Reflex tachycardia
  - Miosis
  - Nasal congestion
- Histamine receptor effects
  - Sedation
  - Hypotension
  - Appetite stimulation
- Cardiac receptor effects
  - QTc interval prolongation
  - Torsades de pointes
  - QRS prolongation
- Serotonin receptor effects
  - Headache
  - Agitation
  - Nausea
  - Diarrhea

Modified from Scheurer D. et al. *Restrained Use of Antipsychotic Medications: Rational Management of Irrationality*. 2012. **Independent Drug Information Service**.

Treatment- Bipolar Depressive Episode

- ✓ Stop Antidepressants
  - Antidepressants can **worsen** depression in bipolar disorder
- ✓ Lithium (Lithobid, etc.)
- 3. Quetiapine (Quetiapine)

Can treat both depression AND hypomania/mania

4. Lamotrigine (Lamictal)
5. Lurasidone (Latuda)
6. Combination therapy

Remember- when choosing a treatment, aim for monotherapy and a medication that can treat multiple phases of the disorder

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Treatment- Bipolar Depressive Episode

But what about Valproate (Depakote)?

A few **small** studies show effectiveness in ACUTE bipolar depression but:

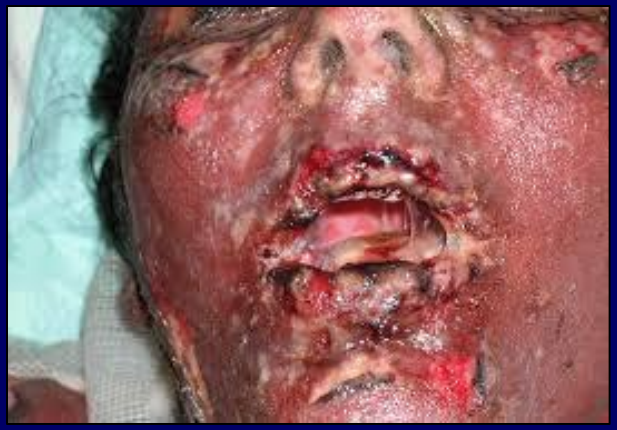
- It's not FDA approved
- It's not effective for maintenance treatment of depression or mania

Quetiapine (Seroquel)

- Effective for manic/hypomanic and depressed episodes
- Generally need dose of 300-600mg for adequate treatment
- Baseline labs- CBC, LFTs, weight, waist circumference, EKG (QTc), HbA1c, fasting glucose, fasting lipid profile
- NOT first choice due to Side Effects:
- Sedation
- Metabolic effects: MASSIVE weight gain, DM II, hyperlipidemia, increased appetite
- Dizziness, hypotension, headache, agitation
- Note: Seroquel is now being abused recreationally
  - Known as “Quell", "Snoozeberries", or "Susie-Q”

Lamotrigine (Lamictal)

- Only helpful for depressive episodes
- Risk for Steven-Johnson's so need to titrate very slowly
  - Risk is highest during dose increases
- Typical titration:
  - 12.5 mg daily x 2 weeks
  - 25mg daily x 1-2 weeks
  - 25mg BID x 1 week
  - 50mg BID x 1 week
  - 100mg BID x 1 week
  - Etc.



- Generally need doses of 150+mg for effectiveness
- Can check a serum level

Jangir SN et al. *Lamotrigine is said to be safe but be cautious: a case report*. **IJCRI** 2011: 2(12) 19-22.

Lurasidone (Latuda)

- New atypical antipsychotic
- Side Effects
  - MUCH less risk for weight gain and metabolic side effects
  - Small risk for akathisia and QTc prolongation (not as bad as with ziprasidone)
  - Needs to be taken with 350 cal of food to absorb it properly
- Shown to be effective for treatment of bipolar depression
- No studies published yet on effectiveness for mania but will likely be effective like all other atypical antipsychotics

Monitoring for Patients Taking Antipsychotics

	Baseline	4 Weeks	8 Weeks	12 Weeks	Quarterly	Annually
Personal & Family Hx	X					X
Weight (BMI)	X	X	X	X	X	
Waist Circ.	X					X
Blood Pressure	X					X
Fasting Plasma Glucose	X					X
Fasting Lipid Profile	X					X

Modified from Scheurer D. et al. *Restrained Use of Antipsychotic Medications: Rational Management of Irrationality*. 2012. **Independent Drug Information Service**.

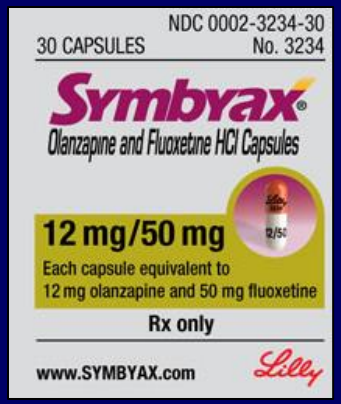
What about other Antipsychotics for Bipolar Depression?

- Other antipsychotic medications are NOT effective for bipolar depression!

Ansari A & Osser D. *The Psychopharmacology Algorithm Project at the Harvard South Shore Program: An Update on Bipolar Depression.* 2010. **Harv Rev Psychiatry.** 36-55.

What about using OFC (Symbyax)?

- Olanzapine (Zyprexa) / Fluoxetine (Prozac) combination
  - FDA approved for bipolar depression
  - **NOT recommended**
    - Olanzapine
      - Significant metabolic side effects
      - Only Clozapine causes more weight gain than olanzapine!
    - Fluoxetine
      - Can cause irritability or switch into mania/hypomania.
      - Has a long half-life.
        - Active metabolite has elimination half-life of up to 16 days!



Case 3 - Charlie

- ID: 52 yo male car mechanic brought to clinic by his wife
- CC: "I feel great! I don't need to be here."
- HPI:
  - Mood is "fantastic".
  - Stopped his lithium "because I feel great! I don't need that stuff."
  - Has not been to work in days. "I'm going to start my own business! I know exactly how to do it- I'm going to start my own bar and strip club!"
  - Sleeping ~1 hour per night, if that.
  - Driving motorcycle to various strip clubs.
  - Maxed out credit card; Used it to purchase a car for one of the strippers. His wife is quite displeased.

www.blogs.guardian.co.uk

Case 3 - Charlie

- PMHx:
  - Long history of bipolar I with both manic and depressive episodes
  - Hypertension
  - Obesity
  - Hyperlipidemia
  - Diabetes mellitus type II
- Exam:
  - Speech is rapid, difficult to interrupt, flight of ideas.
  - He is not psychotic or suicidal.
  - Drug screen is negative.
- Other issues:
  - Charlie's wife is comfortable taking him home if medication is re-started.
  - His insurance was changed and they cannot afford to pay for hospitalization.
  - Charlie has some insight
    - He agrees that his recent behavior was out of character
    - He agrees to take medication again.

You agree to treat him as an outpatient.

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Treatment- Mania/Hypomania

- For acute agitation- use lorazepam
- Stop antidepressants!
- Ideally want something to treat both manic and depressed phases of the disorder

Mohammad O & Osser D. The *Psychopharmacology Algorithm Project at the Harvard South Shore Program: An Algorithm for Acute Mania.* 2013. **Harv Rev Psychiatry.** In Press.

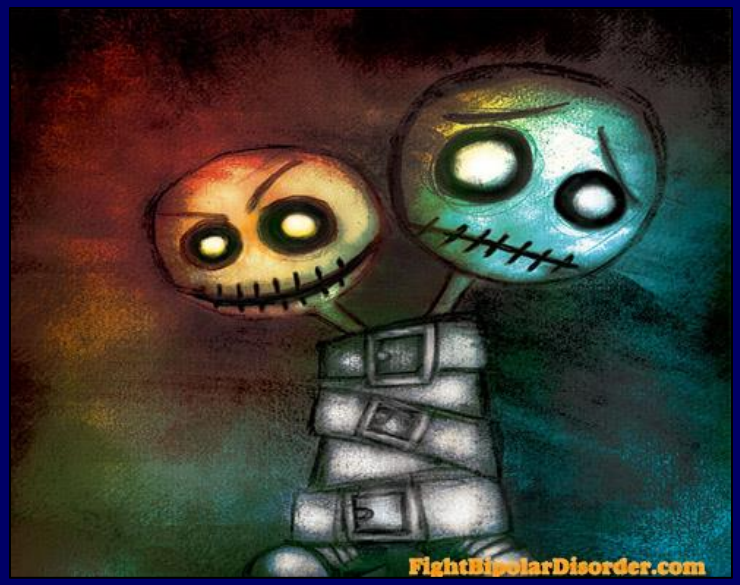
Treatment- Mania/Hypomania

1. Lithium (also good for depression!)
   - Abrupt discontinuation of lithium can lead to a bipolar episode
2. Quetiapine (also good for depression!)
3. Other SGA
   - If QTc is ok, would try ziprasidone (Geodon) first
   - Aripiprazole (Abilify) DOES cause weight gain and can cause significant akathisia
   - An antipsychotic is not the best choice for Charlie due to his PMHx.
   - If psychosis if present you will need to use an antipsychotic medication
   - Avoid giving 2 antipsychotics at once
4. Refer to Psychiatry

Mohammad O & Osser D. The *Psychopharmacology Algorithm Project at the Harvard South Shore Program: An Algorithm for Acute Mania.* 2013. **Harv Rev Psychiatry.** In Press.

DSM-V New Bipolar Disorder Specifiers

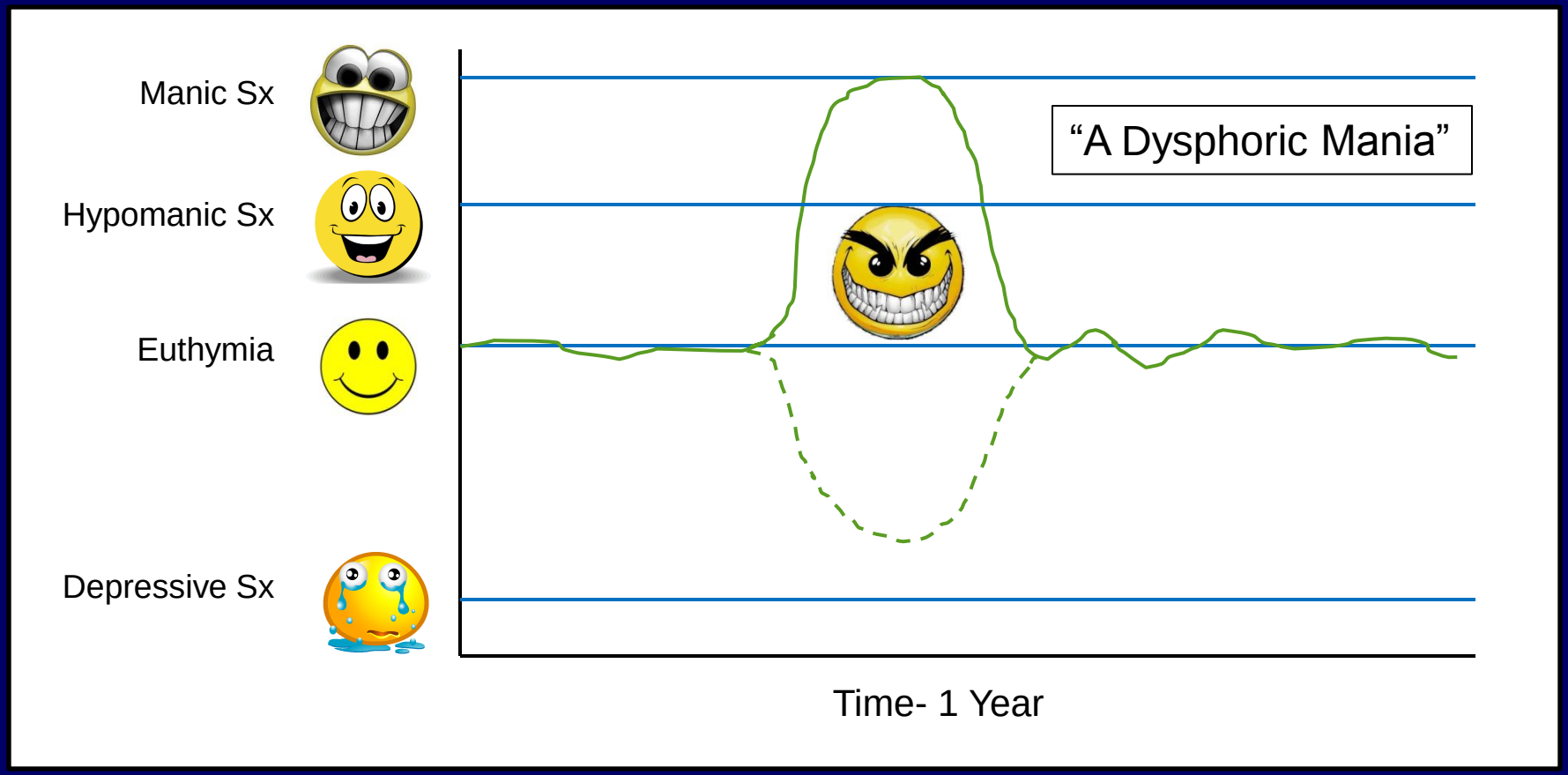
- **With mixed features**
  - Manic/hypomanic episode, with mixed features
  - Depressive episode, with mixed features
- VERY uncomfortable phases of bipolar disorder
- IMPORTANT because TREATMENT DIFFERS



DSM-V Bipolar Disorder Specifiers

- Manic or hypomanic episode, with mixed features:
  - Full criteria are met for a manic episode or hypomanic episode
    - 3 + Depressive Symptoms
      1. Prominent dysphoria or depressed mood
      2. Diminished interest or pleasure in all, or almost all, activities
      3. Psychomotor retardation nearly every day (observable by others; not merely subjective feelings of being slowed down).
      4. Fatigue or loss of energy.
      5. Feelings of worthlessness or excessive or inappropriate guilt
      6. Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

DSM-V- Manic/Hypomanic Episode with Mixed Features



Case 4 - Margaret

- ID: 58 yo woman found in clinic parking lot yelling at the cab driver- "I won't pay you! You work for Satan!"

- CC: "God said to come here- that you can help me with my meds. Meds meds heads heads deads dead dead. I don't want to be dead. Elvis is dead. Napoleon is dead. Napoleon was short. Have you ever been to France? I like French fries.

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Case 4 - Margaret

- HPI:
  - Long history of bipolar disorder, both manic and depressive episodes
  - No showed her last 2 appointments.
  - She reports taking her medication.
  - Hasn't slept for 8 days.
  - Tells you she is writing an opera and God has been telling her what lyrics to use for the songs.
  - Denies suicidal or homicidal ideation.
  - She hasn't showered in the past week and has not eaten in the past 3 days.

- PMHx: Bipolar I disorder, diabetes mellitus II, history of myocardial infarction, hypertension, hyperlipidemia, GERD
- Exam: Pressured speech, psychomotor agitation, very distractible, appears very energized and angry

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Bipolar Manic/Hypomanic Episode with Mixed Features

- Lorazepam for acute agitation. (Would recommend hospitalization for Margaret!)
- MUST stop antidepressants
- 1st Choice Atypical antipsychotic (even if psychosis is not present)
  - Best evidence for aripiprazole (Abilify) and ziprasidone (Geodon)
  - Quetiapine (Seroquel) is also good and treats later depressive episodes but may need HIGH doses to treat the mania
- 2nd- ADD divalproex (Depakote)
  - Monitor LFTs
  - Risk for weight gain, hair loss, potentially fatal hepatopancreatitis
- 3rd- ADD lithium
- Refer to Psychiatry
- 4th could consider carbamazepine (Tegretol) but low effect sizes, many drug-drug interactions, little maintenance data
- AVOID giving 2 antipsychotics

Mohammad O & Osser D. The *Psychopharmacology Algorithm Project at the Harvard South Shore Program: An Algorithm for Acute Mania.* 2013. **Harv Rev Psychiatry.** In Press.

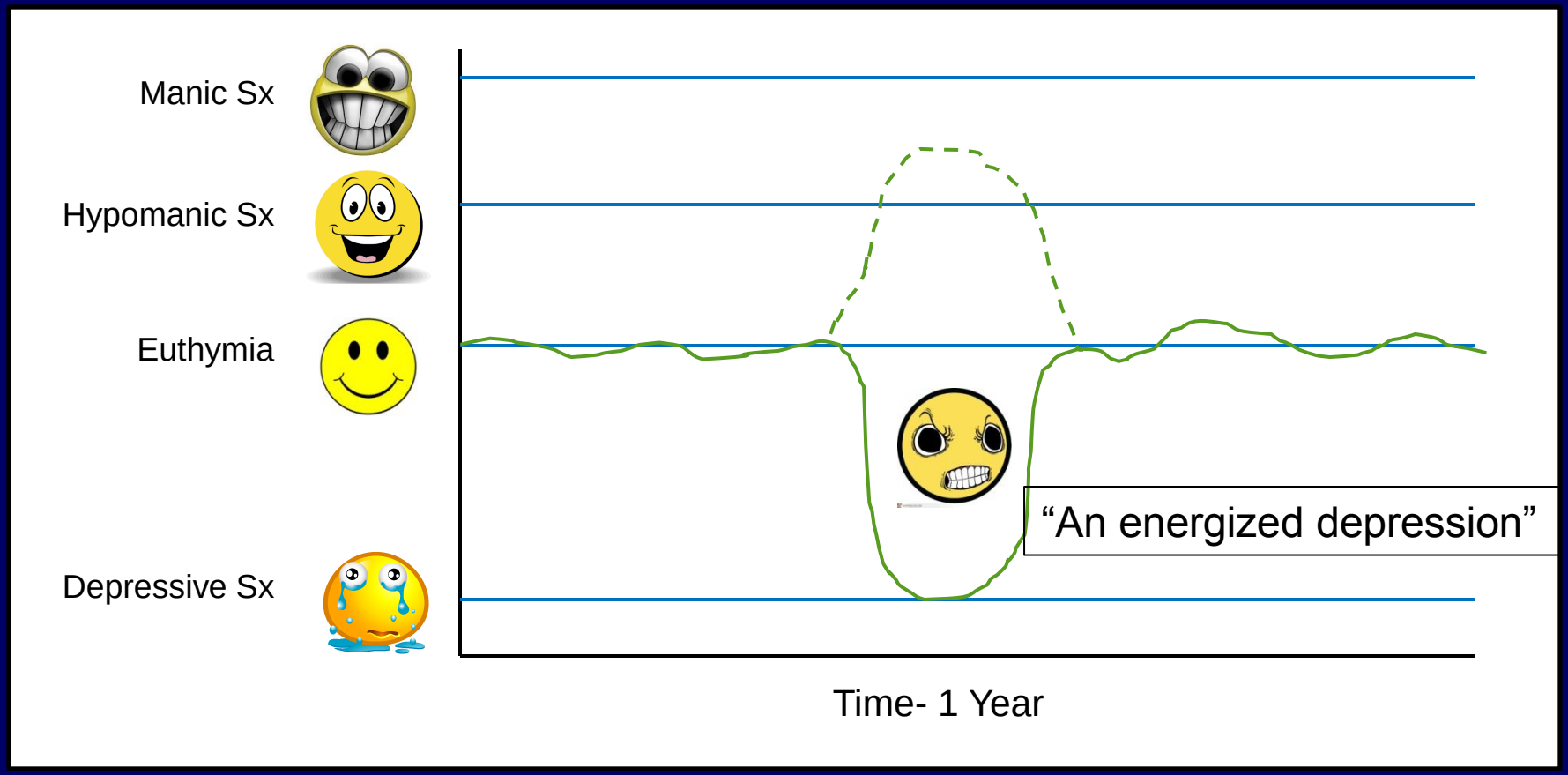
Bipolar Manic/Hypomanic Episode with Mixed Features

- This is the only phase of bipolar disorder in which:
  - SGA is the first choice treatment
  - Divalproex (depakote) is better than lithium

DSM-V Bipolar Disorder Specifiers

- Depressive episode, with mixed features:
  - Full criteria are met for a major depressive episode
    - 3 + manic/hypomanic symptoms
      1. Elevated, expansive mood.
      2. Inflated self-esteem or grandiosity.
      3. More talkative than usual or pressure to keep talking.
      4. Flight of ideas or subjective experience that thoughts are racing.
      5. Increase in energy or goal-directed activity.
      6. Increased or excessive involvement in activities that have a high potential for painful consequences
      7. Decreased need for sleep (feeling rested despite sleeping less than usual; to be contrasted with insomnia).

DSM-V- Depressive Episode with Mixed Features



Back to Case 1 - Brad

- ID: 18 year old male high school senior from Central Maine brought to PCP by his mother
- HPI:
  - 3 week history of:
    - depressed mood
    - poor sleep
    - increased energy
    - anhedonia
    - problems concentrating
    - Reports intermittent suicidal ideation without plan or intent
- PMHx: None
- FamHx: Mom with Bipolar II Disorder

Back to Case 1 - Brad

- Further discussion reveals…
  - Reports having racing thoughts
  - Talking faster than usual
  - Appears to be very irritable
  - Episodes of anger and rage
    - Recently destroyed his room and frightened his mom
      - Very out of character
  - Increased sex drive recently
    - Looking at porn online
      - Out of character
  - Speeding ticket
    - Driving 70 mph on a back road in Central Maine
      - Out of character

Bipolar Depressed Episode with Mixed Features

1. Lithium
2. Quetiapine (Seroquel)
3. Lamotrigine (Lamictal)
4. Consider ziprasidone- study suggests it could be helpful in this form of bipolar depression
5. Refer to Psychiatry

Address Comorbidities

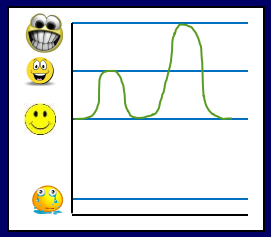
- Alcohol dependence
  - Consider medication for cravings
    - Naltrexone, topiramate, naltrexone
    - Avoid Antabuse
    - Refer to Alcoholics Anonymous or Smart Recovery
- PTSD
  - Prazosin titration
- Anxiety
  - Avoid SSRIs which can switch into mania, worsen depression, or cause irritability
  - Refer for psychotherapy when possible

When Should I Refer to Psychiatry?

- Emergency Evaluation
  - Suicidal or homicidal ideation
  - Other danger to self or others
    - Lack of self-care
    - Poor judgment due to psychosis
- Pregnancy
- First few medication trials are not effective / Treatment resistance
- Combination therapy is needed

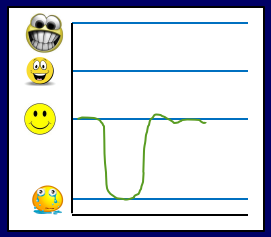
Treatment of Bipolar Disorder

Bipolar Manic/Hypomanic Episode



1. Stop antidepressants
2. Lithium (Level > 0.8; Also treats depression)
3. Quetiapine (also treats depression)
4. Other atypical (ziprasidone, risperidone)
5. Consider valproate but not effective for maintenance treatment

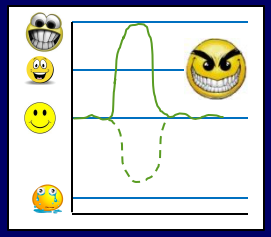
Bipolar Depressive Episode



1. Stop antidepressants
2. Lithium (acute level > 0.8; Maintenance 0.6-0.75)
3. Quetiapine
4. Lamotrigine
5. Lurasidone

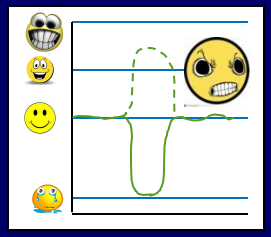
Do NOT use OFC
Other SGAs are not effective
Carbamazepine and valproate not effective

Bipolar Manic/Hypomanic Episode with Mixed Features



1. Stop antidepressants
2. Atypical antipsychotic (best choice is quetiapine)
3. Add divalproex
4. Add lithium Lithium (level > 0.8)

Bipolar Depressive Episode with Mixed Features



1. Stop antidepressants
2. Lithium (level > 0.8)
3. Quetiapine
4. Lamotrigine
5. Ziprasidone

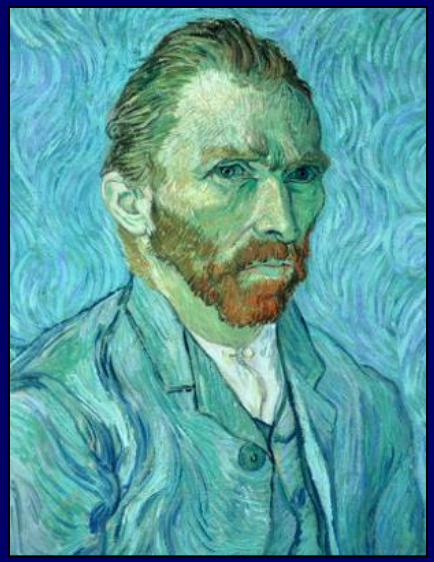
Ansari A & Osser D. *The Psychopharmacology Algorithm Project at the Harvard South Shore Program: An Update on Bipolar Depression.* 2010. **Harv Rev Psychiatry.** 36-55.
Mohammad O & Osser D. The *Psychopharmacology Algorithm Project at the Harvard South Shore Program: An Algorithm for Acute Mania.* 2013. **Harv Rev Psychiatry.** In Press.

Learning Objectives

- ✓ Understand epidemiology of bipolar disorder in the general population and in primary care practice.
- ✓ Understand new DSM criteria for bipolar disorder.
- ✓ Understand how to prepare a primary care practice to treat patients with bipolar disorder
- ✓ Understand how to diagnose bipolar disorder in the primary care setting.
- ✓ Understand safety assessment in the primary care setting.
- ✓ Understand evidence-based treatments for the various phases of bipolar disorder and be able to implement these treatments in the primary care setting.
- ✓ Understand when the use of antipsychotic medication is indicated.
- ✓ Understand the assessment and treatment of common comorbidities of bipolar disorder in the primary care setting.
- ✓ Understand when patients should be referred to a psychiatrist.

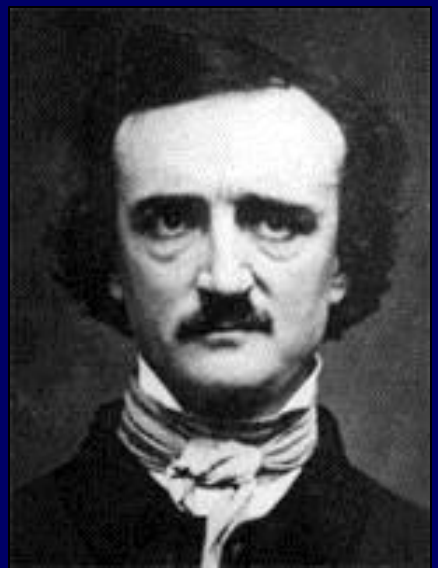
Famous People with Bipolar Disorder??

Vincent van Gogh



Marilyn Monroe

Edgar Allen Poe

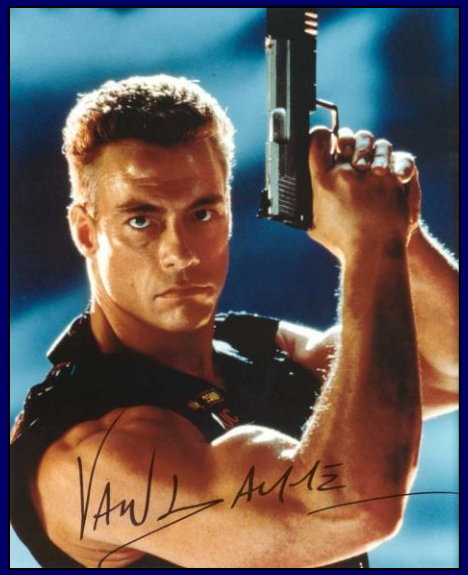


Frank Sinatra

http://en.wikipedia.org/wiki/List_of_people_with_bipolar_disorder
www.famousbipolarpeople.com

Famous People with Bipolar Disorder??

Jean-Claude Van Damme



Carie Fisher

Sinead O'Connor

Linda Hamilton

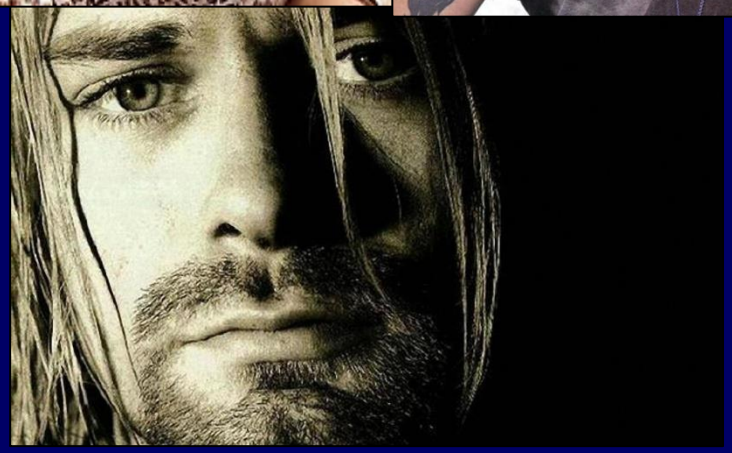
http://en.wikipedia.org/wiki/List_of_people_with_bipolar_disorder
www.famousbipolarpeople.com
www.health.com

Famous People with Bipolar Disorder??

Macy Gray

Axl Rose

Kurt Cobain



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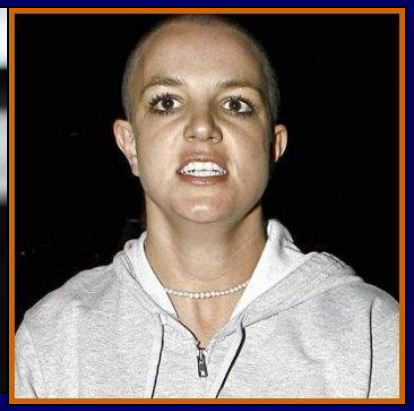
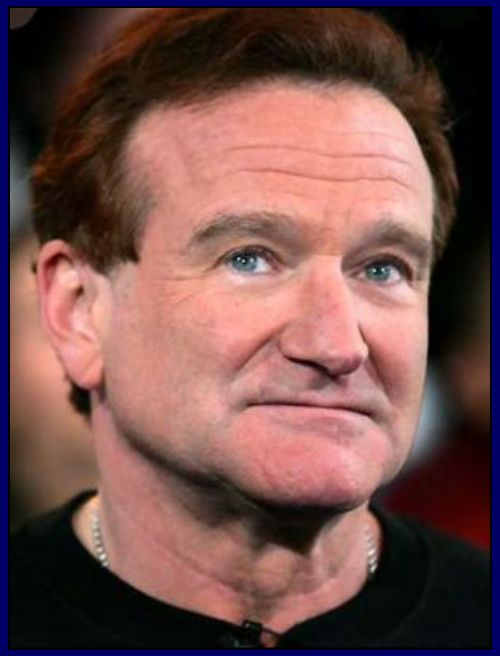
Famous People with Bipolar Disorder??



Britney Spears

Catherine Zeta-Jones



Robin Williams

http://en.wikipedia.org/wiki/List_of_people_with_bipolar_disorder
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www.health.com

References

1. Ansari A & Osser D. *The Psychopharmacology Algorithm Project at the Harvard South Shore Program: An Update on Bipolar Depression.* 2010. **Harv Rev Psychiatry.** 36-55.
2. Culpepper L. *The Role of Primary Care Clinicians in Diagnosing and Treating Bipolar Disorder*. **Prim Care Companion J Clin Psychiatry.** 2010; 12(Suppl 1): 4–9.
3. Feldman et al. *Do Patient Requests for Antidepressants Enhance or Hinder Physicians' Evaluation of Depression?: A Randomized Controlled Trial.* 2006. **Medical Care;** 44(12):1107-1113.
4. Jangir SN et al. *Lamotrigine is said to be safe but be cautious: a case report*. **IJCRI** 2011: 2(12) 19-22.
5. Jefferson JW et al. Lithium Encyclopedia for Clinical Practice 2nd Ed. 1983. American Psychiatric Press Inc.
6. Kilbourne AM et al. *Burden of general medical conditions among individuals with bipolar disorder.* **Bipolar Disorders.** 2004. 6:5, 368-373.
7. Konopaske GT, Dorph-Petersen KA, *Sweet RA, et al. Effect of chronic antipsychotic exposure on astrocyte and oligodendrocyte numbers in macaque monkeys.* 2008. **Biol Psychiatry**; 63:759-65
8. Mohammad O & Osser D. The *Psychopharmacology Algorithm Project at the Harvard South Shore Program: An Algorithm for Acute Mania*. 2013. **Harv Rev Psychiatry.** In Press.
9. Scheurer D. et al. *Restrained Use of Antipsychotic Medications: Rational Management of Irrationality*. 2012. **Independent Drug Information Service**.