



UW PACC

Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

BIPOLAR DISORDERS

DIAGNOSTIC AND TREATMENT ISSUES

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RIES CONFLICT OF INTEREST STATEMENT

- Dr. Ries has Grant funding from:
 - NIH- NIDA- NIMH
 - Contingency Management Alcohol in Mentally Ill
 - Preventing Addiction Related Suicide
 - Prolonged Exposure +/- Sertraline for Severe PTSD
 - Suicide Prevention follow up study- AFSP
 - Use of MAT for Opioid Dep in Primary care
 - PTSD treatment in Heavy MJ users
 - Dept of Defense
 - Suicide prevention in troops
 - Washington State
 - Telemedicine Case Didactics and Case conferences on Psych/Addictions patients in Primary Care (UW PACC)

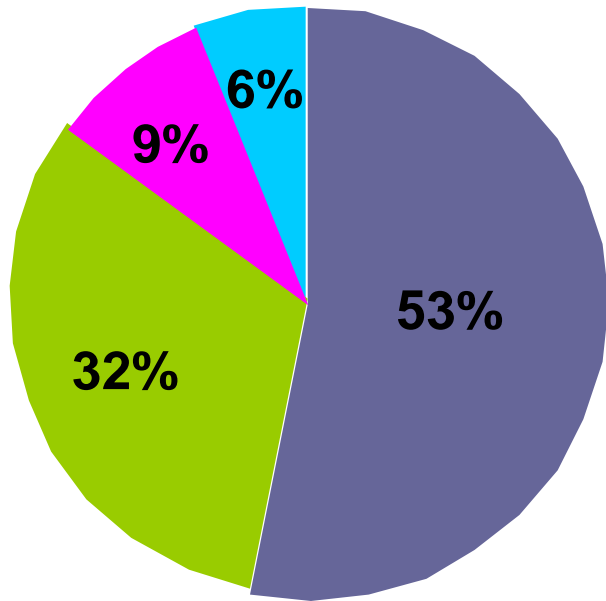
JOANNE...

- Complains of intense fatigue, depression, and sleeping 12+ hrs a day, but when awake feeling terrible anxiety and irritability, then not sleeping for 2 days. She has a history of 2 previous depressions and has been taking sertraline 200 mg a day.
- Family positive for alcohol in father and recurrent severe depression in mother, and grandmother who spent time in state hospital.

TIME SPENT IN SPECIFIC BIPOLAR DISORDER AFFECTIVE SYMPTOMS

Bipolar I Patients

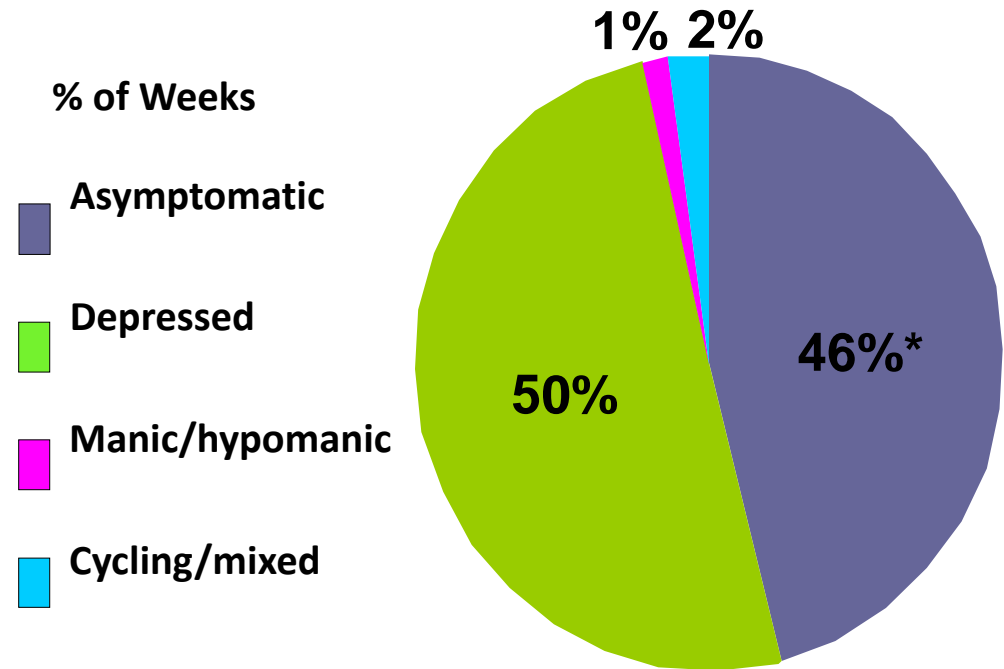
146 bipolar I patients followed 12.8 years



**Ratio of 3:1
Depressed vs Manic/hypomanic**

Bipolar II Patients

86 bipolar II patients followed 13.4 years



**Ratio of 39:1
Depressed vs Hypomanic**

*%s do not add to 100 due to rounding

DIFFERENTIAL DIAGNOSIS: MDD OR BIPOLAR DISORDER?

It may take up to 10 years or more for bipolar disorder to be accurately diagnosed and treated.

Clues that your patient may have bipolar disorder

5. Associated Features

- Unevenness in intimate relationships
- Frequent career changes
- High prevalence of comorbidities (eg, substance use disorders)

4. Mania Symptoms

- Distractibility
- Decreased need for sleep
- Grandiosity / Flight of ideas / Racing thoughts
- Irritability / Risky behavior / Pressured speech

1. Family History

- Higher rates of psychiatric illness
- Positive for bipolar disorder

2. Course of Illness

- Illness onset usually before age 25
- Increased overall mood episodes
- Postpartum onset of depression
- Highly recurrent depressive episodes

3. Treatment Response

- Suboptimal outcome with antidepressants
- Antidepressant-induced manic switch



**Key
Elements**

BIPOLAR MEDICATIONS TREATMENT: MOOD STABILIZERS

Lithium* Bipolar 1 prevention

Anticonvulants

Depakote* (divalproex sodium)

Lamictal* (lamotrigine)- Bipolar 2 prevention

Tegretol (carbamazepine)

Trileptal (oxcarbazepine)

Neurontin (gabapentin) Topamax (topiramate) Keppra (levetiracetam)

Atypical Antipsychotics

Seroquel (quetiapine)

Latuda (Lurasidone)

Zyprexa (Olanzapine) plus antidep.

Abilify (Aripiprazole) plus Mood stabilizer or antidep

*FDA-approved

MOOD STABILIZERS: LITHIUM

- Advantages:
 - 50+ years worldwide experience (FDA-approved 1970)
 - effective in euphoric mania and hypomania
 - inexpensive
 - reduces suicide rate^{1,2}
- Disadvantages:
 - slow onset ~ 14 days
 - narrow therapeutic index
 - non-response in > 50% (usually bipolar subtypes)
 - frequent side effects (polyuria, tremor, GI symptoms) and non-compliance
 - discontinuation associated with high relapse rate³

¹Baldessarini RJ, et al. J Clin Psychiatry. 2003;64 Suppl 5:44-52.

²Goodwin FK, et al. JAMA. 2003 Sep 17;290(11):1467-73.

³Cavanagh J, et al. Acta Psychiatr Scand. 2004 Feb;109(2):91-5.

MOOD STABILIZERS: DIVALPROEX

- Advantages:
 - extensive experience (FDA-approved for epilepsy 1983; for bipolar mania 1995)
 - rapid onset (1-4 days)
 - loading dose strategy¹ well-tolerated:
 - 20 mgs/kg
 - 77% moderate to marked response
 - effective in Bipolar subtypes
 - effective for psychotic symptoms²
 - plasma levels (50-125 mcg/ml)
 - less cognitive impairment than lithium³

MOOD STABILIZERS: DIVALPROEX

- Disadvantages:
 - sedation
 - transient hair loss
 - weight gain
 - tremor
 - GI upset
 - dose-related thrombocytopenia
 - rare hepatotoxicity, pancreatitis
 - possible Polycystic Ovarian Syndrome
 - plasma level monitoring

MOOD STABILIZERS: LAMICTAL

- FDA-approved for *maintenance treatment* of Bipolar I Disorder
- Black box warning for serious rash (includes Stevens-Johnson Syndrome and toxic epidermal necrolysis)
- *Slow titration* necessary
- Interaction with other AEDs (especially valproic acid and carbamazepine)

LAMICTAL: EFFICACY IN BIPOLAR DISORDER

- Placebo controlled 18-month trials of lamotrigine and lithium – pooled analysis
- 8-16 week open label treatment with lamotrigine or lithium before randomization:
 - N = 191 for placebo
 - N = 280 for lamotrigine (100-400 mgs/d)
 - N = 167 for lithium (0.8-1.1 mEq/L)
- 18-month maintenance treatment phase
- Both *lamotrigine and lithium superior to placebo* in preventing any mood episode

Goodwin GM, et al;J Clin Psych 2004 Mar;65(3):432-441

Bowden CL, et al;Arch Gen Psych 2003 Apr;60(4):392-400

Calabrese JR, et al;J Clin Psych 2003 Sep;64(9):1013-1024

WHAT ABOUT BIPOLAR MANIA + PSYCHOSIS MANAGEMENT

- **Acute**
 - Antipsychotic + “mood stabilizer”+ Benzo
 - Example- Olanzapine 20 + Lithium 300 tid + Lorazepam 1 mg tid
- **Subacute** : lower Antipsychotic and the Benzo/ up the lithium, or change to Divalproex
- **Longer term**: Li 600 am and 900 pm with level 0.8 plus aripiprazole (less sedating) or Loxapine 10 mg (more sedating) --- both metabolically lower risk

WHAT ABOUT SEVERE BIPOLAR DEPRESSIONS ?

- Increase Lithium to near toxic levels (1.2)
- Add Lamotragine Bip 2
- Add antidep (bupropion or SSRI)
 - If bipolar 1 and has had full mania or psychosis in history, add antipsychotic before the antidepressant
 - Example --Pt now on Lithium or Divalproate + Aripiprazole 15mg + Bupropion 300 mg
- Add Quetiapine (300 mg) or Lurasidone (40-120)
- Consider ECT in med resistant depressions

COMPARATIVE SIDE EFFECT PROFILE OF ATYPICAL NEUROLEPTICS AND BIPOLAR

Drug:	EPS:	Weight Gain:	Sedation:	Prolactin:
Aripiprazole	0/+	0/+	0/+	0
Lurasidone	0/+	0/+	0/+	0
Olanzapine	++	++++	++	++
Quetiapine	0	++	+++	0
Risperidone	+++	+++	+	+++
Ziprasidone	++	0/+	+	+

IT MAY NOT BE THAT THE MED(S) STOPPED WORKING, BUT.....

- The patient stopped the med...or
- The patient stopped the med AND used drugs and/or alcohol.....
- OR lowered the med and used...
- OR used on top of the med....
- OR used twice the dose on one day and nothing the next....
- Stimulants (cocaine/amphets) are most MSE destructive, but alcohol most suicide related

WHAT ABOUT TALK THERAPY?

- [J Affect Disord.](#) 2016 Sep 1;201:203-14. doi: 10.1016/j.jad.2016.05.018. Epub 2016 May 14.
- **Empirically supported psychosocial interventions for bipolar disorder: Current state of the research.**
- [Salcedo S¹](#), et al

We conducted a search of the literature to examine recent (2007-present), randomized controlled studies

- All of the psychotherapy interventions appear to be effective in reducing depressive symptoms.
- Psychoeducation and CBT are associated with increased time to mood episode relapse or recurrence.
- MBCT (mindfulness based) has demonstrated a particular effectiveness in improving depressive and anxiety symptoms.
- Online psychotherapy interventions, programs combining one or more psychotherapy interventions, and targeted interventions centering on particular symptoms have been the focus of recent, randomized controlled studies in bipolar disorder.

JOANNE ---BIPOLAR TID RECOVERY

EXERCISE:

LINKING BIO-PSYCHO-SOCIAL-

- Three x Three (TID) Times a Day:
 - My Recovery Plan includes (Rx Plan)
 - 1. seeing my prim care doc/nurse every 2 weeks, for now
 - 2. taking my Bipolar meds and hypertension meds every day
 - 3. power walking once a day
 - In order to (Rx Goals)
 - 1. get my health back
 - 2. keep my family together
 - 3. prevent another suicide attempt
 - And Three things I am grateful for include: (Gratitude)
 - 1. I have my family and job
 - 2. Bipolar meds work if you take them and don't drink
 - 3. I am way better than last Spring...there is Hope

CASE PRESENTATION

- George is a 32 yo single primary care patient who recently joined your practice. His physical exam and screening labs are normal other than slight hyperlipidemia. His mental status is normal.
- History reveals that George has had previous treatment for depression with a hospitalization in California 3 years ago and outpatient treatment 5 years ago.
- He does not remember the medications he took 5 years ago, but says he gradually got better. When he was hospitalized he was treated with Venlafaxine 300 mg and clonazepam 2 mg a day which he has continued.

GEORGE

- His primary care doctor asks about why he was taking the clonazepam, and George says it was because that while his depression eventually got better, he also became so agitated that he needed it, however several other doctors have not wanted to prescribe this, and he is also concerned about dependence on it. George tells you that he thinks he might be bipolar because he took an online test and his score indicated that he was bipolar.
- Family history indicates a brother with recurrent depressions and homelessness, who at times acts “very strangely”
- What should his primary care doctor do?