Common Presentations in Primary Care: Bipolar Disorder

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Disclosure Statement:

Relevant financial relationships in the past 12 months

- Consultant/Speaker: None

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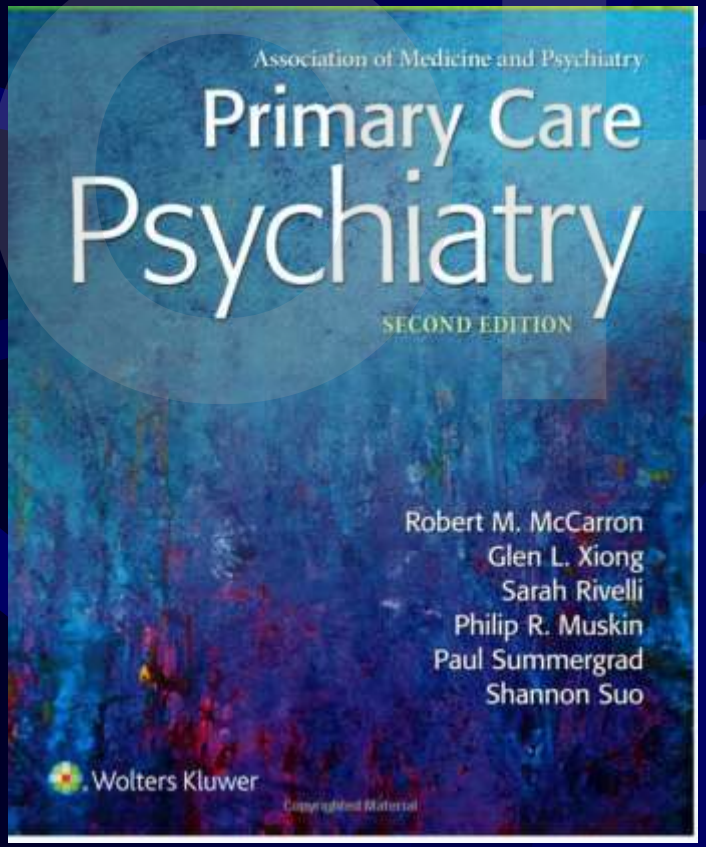
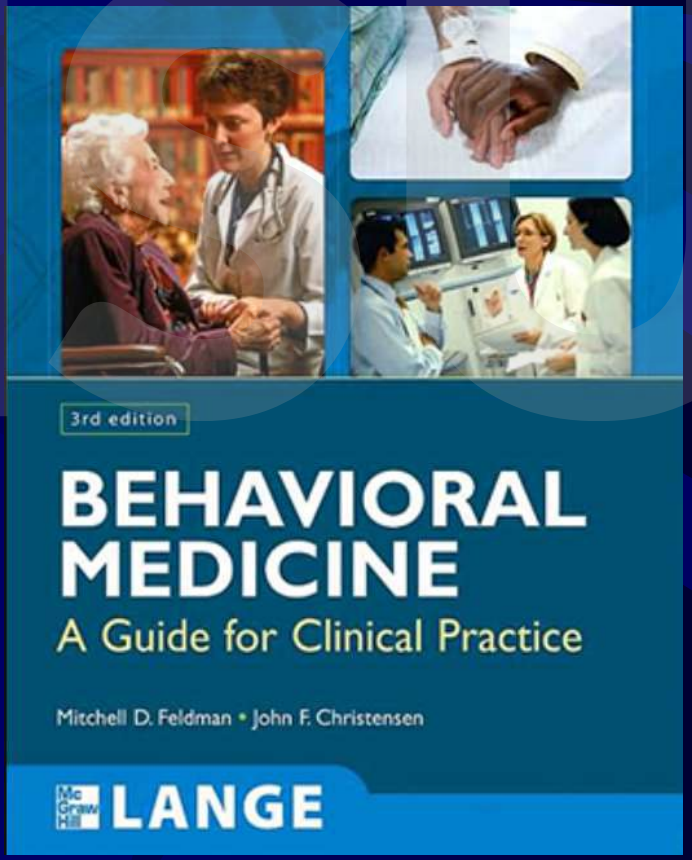
Disclosure Statement:

Relevant financial relationships in the past 12 months

- Bipolar Disorder



- Depression

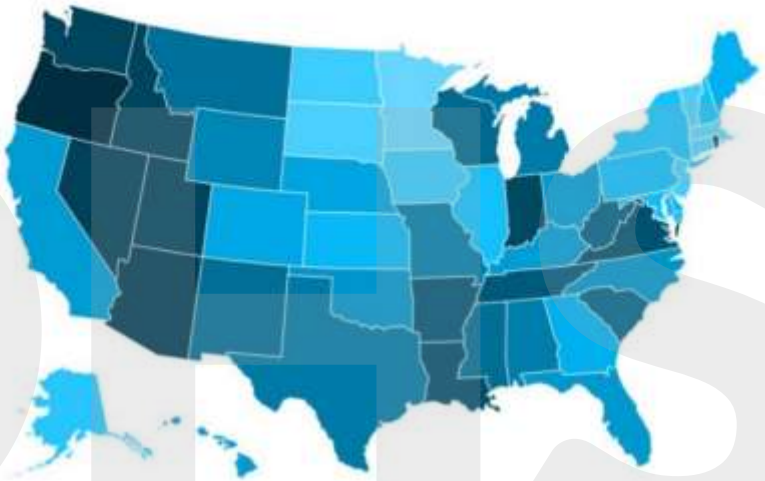


What does a "Med-Psych" Doc do anyways?

State of Mental Health in America 2016-17

Overall Ranking

States that rank in the top ten are in the Northeast and Midwest, while most states that rank in the bottom ten are in the South and the West.



Overall Ranking

Rank	State
1	Minnesota
2	Massachusetts
3	Connecticut
4	Vermont
5	South Dakota
6	New Jersey
7	North Dakota
8	Iowa
9	Alaska
10	New York
11	New Hampshire
12	Illinois
13	Maryland
14	Pennsylvania
15	Kansas
16	Delaware
17	Maine

Rank	State
18	Georgia
19	Colorado
20	Nebraska
21	Kentucky
22	Hawaii
23	California
24	Ohio
25	Florida
26	Oklahoma
27	North Carolina
28	DC
29	Wyoming
30	Missouri
31	Alabama
32	Michigan
33	Texas
34	Montana

Rank	State
35	Mississippi
36	New Mexico
37	Wisconsin
38	South Carolina
39	West Virginia
40	Tennessee
41	Arkansas
42	Virginia
43	Louisiana
44	Indiana
45	Idaho
46	Utah
47	Washington
48	Rhode Island
49	Nevada
50	Arizona
51	Oregon

The Emotional Wellness Center

Finalist, AABH Program of the Year 2018

Monday-Friday 8:30-5pm

Officially Opened: June 12, 2017

"We want it to be inviting and warm and not as, maybe … psychiatric, if I can put it that way," said Raj. "Sometimes psychiatric, we think cold, Spartan, let's not do damage to anything. Here, patients say, 'I can function normally. I do belong in an office, not in a place with a bed and four walls.'"

- The Lund Report

How Many of You Busy Clinicians Feel Comfortable Managing Bipolar Disorder?

Why A Review of Bipolar Disorder Should Matter To You

- Nearly 74% of people seeking help for depression are treated by their primary care physician
- 60% of people with bipolar disorder are in the depressed phase when they go to their primary care doctor for help
- Up to 30% of primary care patients treated for depression and/or anxiety actually have bipolar disorder

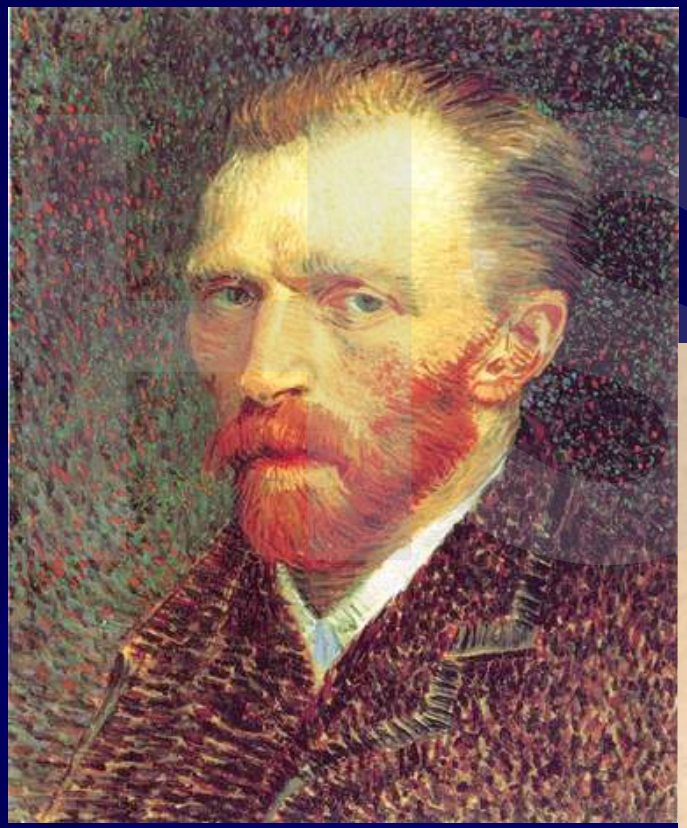
» USPSTF and AAFP data

Why A Review of Bipolar Disorder Should Matter To You

The risks of uncontrolled or untreated bipolar disorder are severe:

- Neurological deterioration
- Suicide and suicide attempts*
- Relapse and hospitalization
- Impact on relationships
- Impact on employment

Famous Persons with Bipolar Disorder



Another “Face” of Bipolar Illness

An Unquiet Mind

- *"The Chinese believe that before you can conquer a beast you first must make it beautiful."*
- *"It has been a fascinating, albeit deadly, enemy and companion; I have found it to be seductively complicated, a distillation both of what is finest in our natures, and of what is most dangerous."*

» *Kay Redfield Jamison*

Outline

- Overview
- Screening/Diagnosis
- Pharmacotherapy: The highlights
- Metabolic Concerns
- Suicide Risk – and ways to minimize your liability

Overview: Mood Patterns

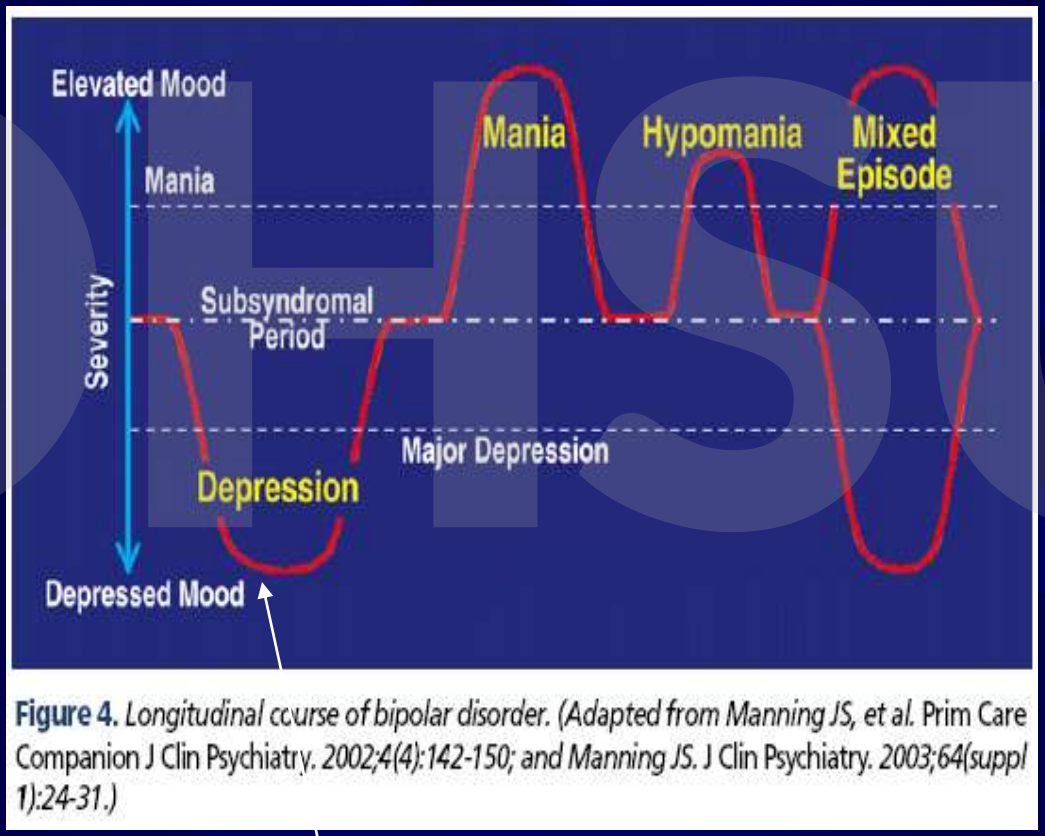


Figure 4. *Longitudinal course of bipolar disorder. (Adapted from Manning JS, et al.* Prim Care Companion J Clin Psychiatry. *2002;4(4):142-150; and Manning JS.* J Clin Psychiatry. *2003;64(suppl 1):24-31.)*

Where most primary care physicians catch BPAD

Overview: Flavors

Bipolar Affective Disorder comes in many flavors:

- Bipolar 1 Disorder: Single Manic Episode, Most Recent Episode Hypomanic, Most recent Episode Manic, Most Recent Episode Mixed, Most Recent Episode Depressed, Most Recent Episode Unspecified
- Bipolar 2 Disorder: Recurrent Major Depressive Episodes with Hypomanic Episodes

  – All can be with or without psychotic features

Mania vs. Hypomania

- Manic Episode – 1 week of elevated, expansive, or irritable mood
  - Three or more must be met:
    - Distractibility – poor focus
    - Insomnia – decreased need for sleep
    - Grandiosity - inflated self-esteem
    - Flight of ideas – racing thoughts
    - Activity – increased goal-directed activity
    - Speech – pressured or more talkative
    - Thoughtlessness – “risk-taking” behavior

Mania vs. Hypomania

- Hypomanic Episode
  - At least 4 days of elevated, expansive, or irritable mood clearly different from the usual non-depressed mood
  - The episode carries the same 3/7 possible symptoms for mania BUT the episode is not severe enough to cause marked impairment in social or occupational functioning, or to necessitate hospitalization

Diagnosis

Mood Disorder Questionnaire (MDQ)

MOOD DISORDER QUESTIONNAIRE (MDQ)

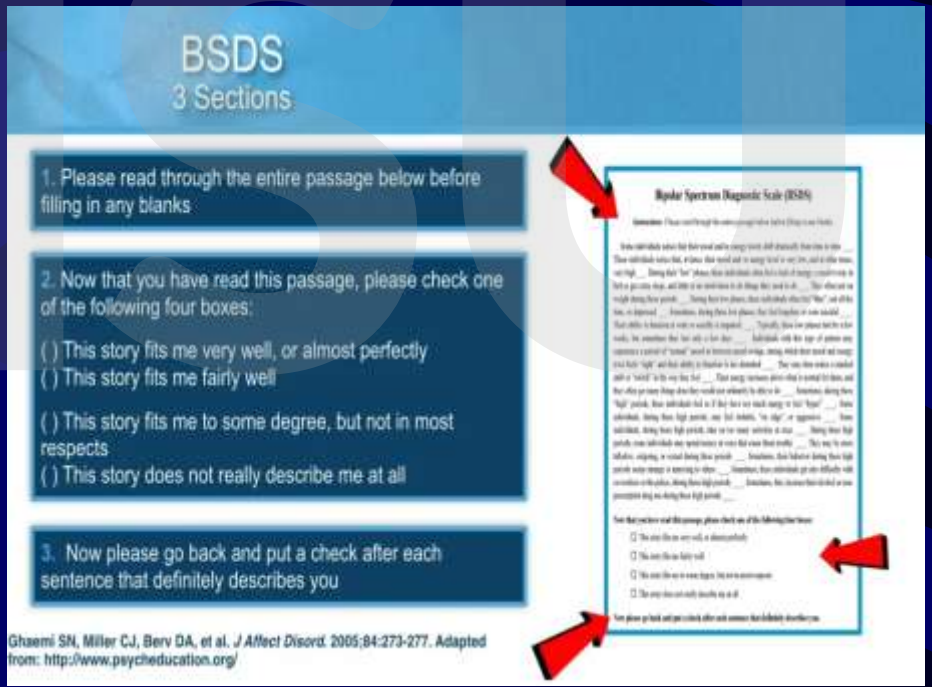
INSTRUCTIONS:

Please answer each question as best you can.

		Yes	No
1	Has there ever been a period of time when you were not your usual self and ...		
	– 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 that you didn't really miss it?	☐	☐
	– you were more talkative or spoke much 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 in trouble?	☐	☐
2	If you checked YES to more than one of the above, have several of these ever happened during the same period of time?	☐	☐
3	How much of a problem did any of these cause you–like being unable to work; having family, money or legal trouble; getting into arguments or fights?		

☐ No problem ☐ Minor problem ☐ Moderate problem ☐ Serious problem

Bipolar Spectrum Diagnostic Scale (BSDS)



BSDS

3 Sections

1. Please read through the entire passage below before filling in any blanks

2. Now that you have read this passage, please check one of the following four boxes:

( ) This story fits me very well, or almost perfectly
( ) This story fits me fairly well
( ) This story fits me to some degree, but not in most respects
( ) This story does not really describe me at all

3. Now please go back and put a check after each sentence that definitely describes you

Ghaemi SN, Miller CJ, Berv DA, et al. *J Affect Disord.* 2005;84:273-277. Adapted from: http://www.psycheducation.org/

Bipolar Spectrum Diagnostic Scale

- Sensitivity of the BSDS was 0.76 - approximately equal in bipolar I and II/NOS which some experts argue make it superior to the Mood Disorder Questionnaire (MDQ) by Hirschfield et al (2001)
  - » Zimmerman M et al. *J Clin Psychiatry*. 2004;65: 605-610.
- The BSDS identified 85% of unipolar-depressed patients as not having bipolar spectrum illness.
  - » Journal of Affective Disorders 2005 Feb;84 (2-3): 273-277

Bipolar "Rule of Threes"

- If the patient has had 3 jobs, 3 marriages, or has failed more than 3 different antidepressants, suspect bipolar disorder

- Remember: irritability can be a mania equivalent

Pharmacotherapy: Treat or Refer?

- Really depends on your comfort level.
- How good are you at:
  - Psychoeducating your patients (‘meducation’)
  - Monitoring drug levels, etc.
- Patients who need immediate stabilization may deserve immediate referral to a specialist

Therapy: Is Lithium Still an Option?

- In the USA, prescription of lithium for outpatients nearly halved between 1992 and 1996, and 1996 and 1999, whereas the rate of prescription of valproate almost tripled.

» Blanco C, Laje G, Olfson M, Marcus SC, Pincus HA. Trends in the treatment of bipolar disorder by outpatient psychiatrists. *Am J Psychiatry* 2002; **159:** 1005–10.

BALANCE trial

- Aim was to establish whether lithium plus valproate was better than monotherapy with either drug alone for relapse prevention in bipolar I disorder.
- Open-label design for lithium monotherapy (plasma concentration 0.4–1.0 mmol/L, n=110), valproate monotherapy (750–1250 mg, n=110), or both agents in combination (n=110). Followed for up to 24 months.
- Result: lithium (59% relapse) works just as well as the combination (54%) – and both were superior to valproate monotherapy (69%).

» Geddes JR et al. *Lancet* 2010; 375: 385–95.

General Lithium Augmentation Pearls

- Recap: reduced suicidal behavior (3x less death and 2x less attempts compared to valproate)
  - » Goodwin et al. *JAMA* 2003;290:1467-73.
- Monitor TSH annually while on lithium
- Avoid these meds which increase risk of lithium toxicity: NSAIDS, ACE-I, ARBs, diuretics (thiazide > loop), tetracycline
- Nephrogenic diabetes insipidus – irreversible

Anticonvulsants

- Valproate (Depakote) – increases GABA
  - great for rapid cycling
  - Mild, transient hepatitis seen in 15-30%
  - Blood levels typically 50-100 ug/mL
- Carbamazepine – structurally similar to TCAs
  - Also good for rapid cycling
  - Watch for agranulocytosis (WBC 3K, ANC 1.5K) and LFT increase by three-fold
  - Autoinduction

Lamotrigine

- Bipolar 1, most recent episode depressed
- Several studies showing benefit in combination with other mood-stabilizers
- RCT monotherapy 7 week study showed that lamotrigine 200mg/day had improvement vs placebo (CGI-I response 51% vs 26%) as early as week 3
  - » *J Clin Psychiatry* Feb 1999;60(2):79-88
- Open label continuation (52-week) study showed significant and sustained benefit on MADRS (highlighting depression benefits)
  - » *J Clin Psychiatry* Feb 2004;65(2):204-10.

Lamotrigine Rash

- Rashes that occur within 5 days of initiating treatment are probably not drug-related - the body and immune system typically take several days to mount a true hypersensitivity reaction (Stevens Johnson Syndrome)
- To reduce the potential for rash, gradual up-titration is suggested: 25 mg for the first 2 weeks, 50 mg for Weeks 3 and 4, and increasing to 100 mg and 200 mg in Weeks 5 and 6.
- Drug interactions are particularly important to consider; in particular, the dose of lamotrigine should be halved when used in conjunction with divalproex and doubled when used with carbamazepine.

» Calabrese JR. Presented at the American Psychiatric Association 159th Annual Meeting; May 20-25, 2006; Toronto, Ontario, Canada.

Antipsychotics in Bipolar Mania

Table 4 – FDA-approved indications for pharmacologic management of bipolar mania

Drug	Bipolor mania		Usual dose range (mg)	Comments
	Acute	Maintenance		
Lithium	A	A	600-2400	Usual therapeutic serum range: 0.8-1.2 mEq/L for acute mania; teratogenic potential; requires ongoing monitoring of weight, renal and thyroid function
Divalproex	A	–	750-2000	Usual therapeutic serum range: 50-125 µg/L for acute mania; teratogenic potential; requires ongoing monitoring of weight, CBC count, LFTs, and menstrual history
Divalproex ER	A, B	–	750-2000	Usual therapeutic serum range: 85-125 µg/L for acute mania; teratogenic potential; requires ongoing monitoring of weight, CBC count, LFTs and menstrual history
Carbamazepine XR	A, B	–	800-1600	Possible therapeutic serum range: 4-12 µg/mL; requires ongoing monitoring of weight, CBC count, LFTs, electrolytes; several AEs; teratogenic potential and drug-interaction issues limit usefulness
Chlorpromazine	A	–	200-800	Approval not based on present-day FDA criteria
Olanzapine	A, B, C, D	A	5-20	Sedation; cardiometabolic AEs
Risperidone	A, B, C	–	1-6	Neuromotor AEs; hyperprolactinemia
Risperidone LAI	A	A,C	25-50[a]	May resolve absorption and adherence issues; may be used as monotherapy or in combination with lithium or divalproex; hyperprolactinemia
Quetiapine	A, C, D	C	400-800	Sedation and cardiometabolic AEs
Quetiapine XR	A, B, C	C	400-800	Sedation and cardiometabolic AEs
Ziprasidone	A, B	C	80-160	Cardiometabolic risks reduced
Aripiprazole	A, B, C, D, E	A, C	5-30	Agitation/anxiety; akathisia; cardiometabolic risks reduced
Asenapine	A, B, C	C	10-20	Sublingual formulation only

A, monotherapy; B, mixed states; C, adjunct to lithium or valproate; D, pediatric/adolescent; E, acute parenteral.
CBC, complete blood cell; LFT, liver function test; ER, extended release; XR, extended release; AEs, adverse effects; LAI, long-acting injectable.
[a]Every 2 weeks.

Antipsychotics in Bipolar Depression

Table – FDA-approved indications for pharmacological management of bipolar depression

	Bipolar depression			
	Acute	Maintenance	Dosage range	Comments
Anticonvulsants				
Lamotrigine		A, B	25-200 mg/d	Low starting dose and slow dose titration required to minimize serious skin reactions
Second-generation antipsychotics				
Olanzapine-fluoxetine combination	A, C		6/25-12/50 mg/d	Olanzapine monotherapy may also be effective; sedation; cardiometabolic adverse effects
Quetiapine	A		300 mg/d	Sedation; cardiometabolic adverse effects
Lurasidone	A, D		20-120 mg/d	Adverse-effect profile generally more benign relative to approved alternatives

Effectiveness of Adjunctive Antidepressant Treatment for Bipolar Depression

- STEP-BD found no advantage of adding antidepressants to mood stabilizers in the treatment of bipolar depression without concurrent manic symptoms
  - » Sachs GS et al. N Engl J Med 2007;356:1711-22.
- If lithium was dosed to a serum level of at least 0.8 meq/liter, then the addition of an antidepressant (paroxetine, imipramine) provided no additional benefit in symptom improvement
  - » Nemeroff CB et al. Am J Psychiatry 2001; 158:906–912

Relapse Prevention

Important because of the “Kindling” hypothesis: the more episodes that occur early in the illness, the more frequent and severe the later episodes will be.

And what about brain effects?

Loss of Gray Matter

- Nearly 40% less gray matter volume (prefrontal cortex) in patients with BPAD compared to controls
- This loss of cortical mass may play an important role in the development of mood disorders in general.

» Devets WC et al. Subgenual prefrontal cortex abnormalities in mood disorders. Nature. 1997;386:824-27.

Metabolic Syndrome 277.7

- Where (arguably) the non-psychiatrist has greatest impact on the outcomes of patients with bipolar disorder
- Among psychiatrists, 76% have diagnosed it, but only 28% correctly identified the five NCEP diagnostic criteria.

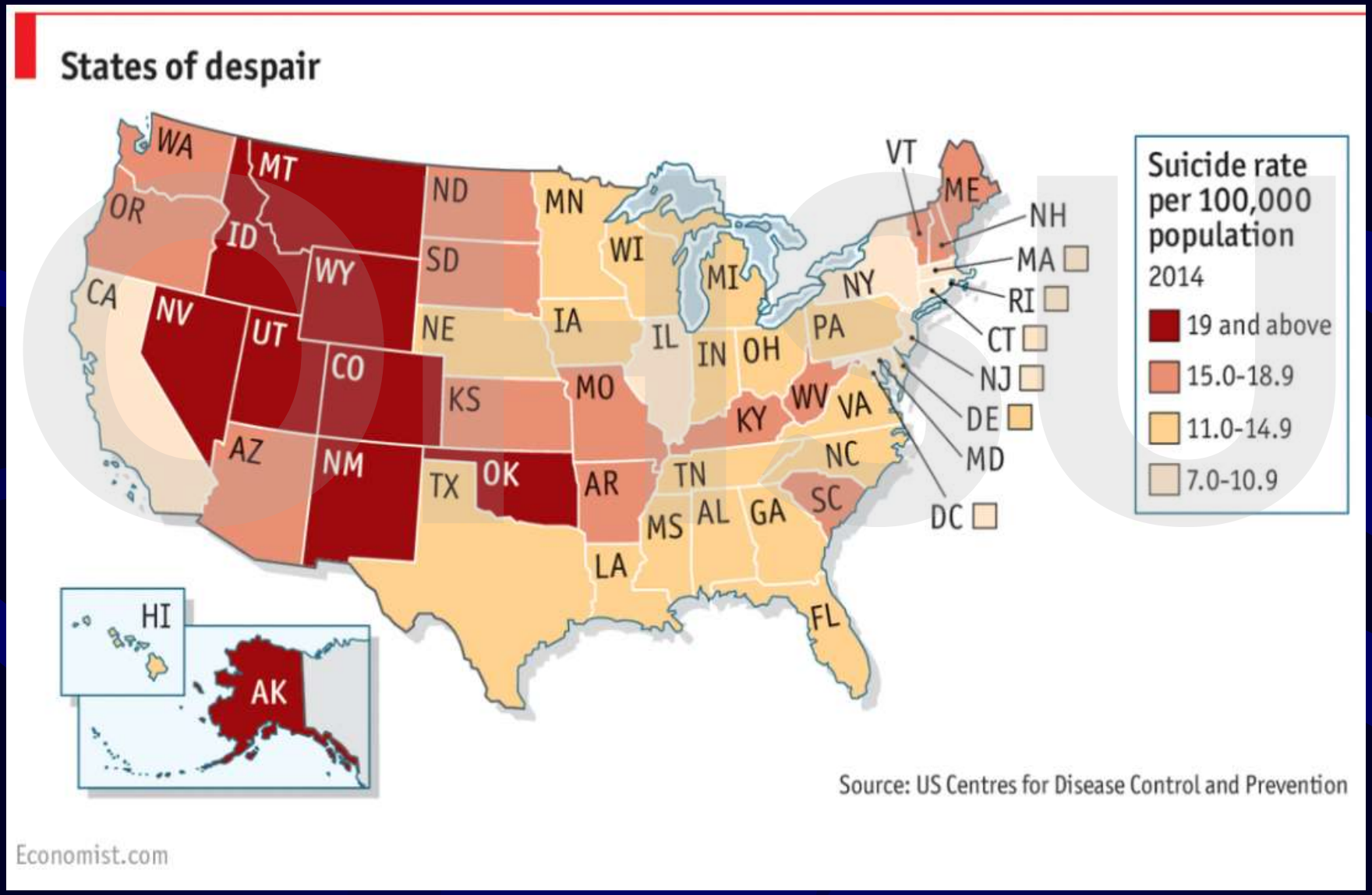
» Psychopharmacology Bulletin. 2007;40(2):22-37.

Metabolic Monitoring

ADA Consensus Development Conference on Atypical Drugs and Obesity and Diabetes[14]

	Baseline	4 Wk	8 Wk	12 Wk	Q 3 Mo	Yearly	Q 5 Y
Personal/family history	X					X	
Weight (BMI)	X	X	X	X	X		
Waist circumference	X					X	
Blood pressure	X		X			X	
Fasting plasma glucose	X		X			X	
Fasting lipid profile	X		X				X

US Suicide Statistics (2014)



Suicide facts: Bipolar Disorder

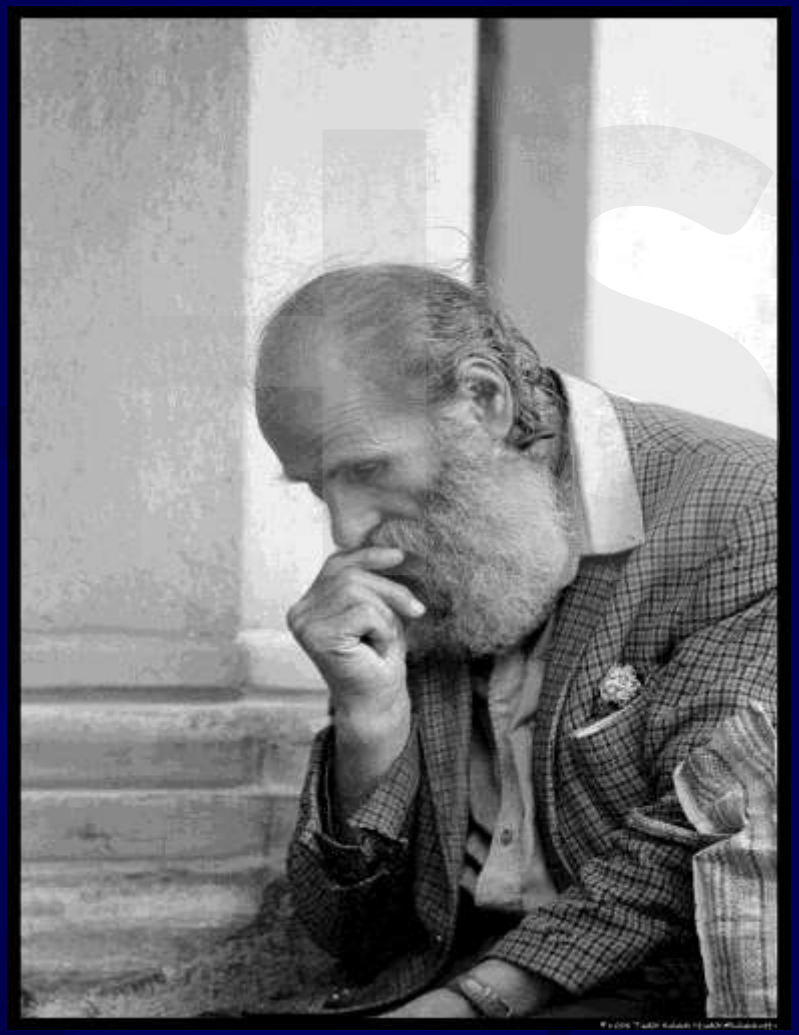
- Bipolar patients have the 2nd highest suicide attempt rate (28.5%) – behind only schizophrenia
- One suicide occurs for every 30 attempts. In bipolar patients, it's 1 suicide for every 3 attempts!

» Baldessarini RJ, et al. Suicide in bipolar disorder: risks and management. CNS Spectr. 2006;11:465-471

- Highest risk factor: male with comorbid anxiety disorder (vs. being young and having a substance-use disorder => predicted attempts but not necessarily suicide)

» Simon GE, et al.. Bipolar Disord. 2007;9:526-530.

The Suicide Assessment



Liability Protection with Suicide

- You are a FM doc whose MA gives you a message about Mrs. S, a 55 yo WW - a patient for 5 years who was prescribed venlafaxine for the past 3 years for "depression." She had self-d/c'd it due to AEs but hadn't felt right in 3 months. You read the message and call in a prescription for escitalopram and have your MA call to tell Mrs. B the plan – with no mention of scheduling an appointment. Mrs. B fills the prescription but the following day takes the entire bottle and fatally hangs herself in the garage. You later hear about the suicide and feel terrible. You don't feel you had anything to do with it until you are served papers by her widower.
  - » Based on a real case as described by Ann Latner, JD

Malpractice

- Plaintiff must prove four elements:
  - A professional duty to the patient
  - Breach of that duty
  - An injury cased by the breach
  - Damages

In this case, not counseling the patient or calling to assess the situation before prescribing another medication would expose you to risk. When in doubt, always schedule a visit.

Systematic Suicide Assessment

- Assess for delirium
- Assess for psychosis – hallucinations
- Assess for mood disorders
- Quote what the patient plans to do – perhaps offer a suggestion if needed
- Collateral from a third party

Summary Statement

- Patient says that she is no longer feeling suicidal. There is no evidence of delirium or psychotic features. She acknowledges her family problems and says that counseling makes sense. She has agreed to a follow-up appointment at the mental health center tomorrow and plans to call her employer today to say she will be back at work next week. She has discussed these plans with her husband who agrees to be seen with her at the initial psychiatric assessment following discharge. Pt no longer needs constant observation.
  - » Goldberg RJ. The Assessment of Suicide Risk in the General Hospital. *General Hospital Psychiatry* 9;446-52, 1987.

Bipolar Summary