

**2009 Strategies for the Recognition and Management of Bipolar Disorder**

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**Please complete the Pretest located in your handout materials prior to the start of the presentation.**

**Thank you!**

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Dr. Montano has served as a consultant for and received honoraria from Astra Zeneca, Eli Lilly and Company, Wyeth, Forest, Sanofi-Aventis, Shire, and Ortho-McNeil. He has received grant/research support from Eli Lilly and Company, Wyeth, Forest, Sanofi-Aventis, and Novartis.

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## Learning Objectives

- Describe important considerations for the diagnosis of bipolar disorder, including identification of prodromal symptoms
- Examine the evidence on the efficacy and safety of pharmacologic and nonpharmacologic treatment strategies in bipolar disorder management
- Understand the economic burdens and barriers to care associated with bipolar disorder

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## Lifetime and 12-Month Prevalence of Bipolar Spectrum Disorder: National Comorbidity Survey Replication

- Nationally representative sample of 9,282 adults (≥ 20 years)
- Direct interviews, Version 3.0 World Health Organization Composite International Diagnostic Interview for assessment of *DSM-IV* lifetime and 12-month Axis I disorders. February 2001–April 2003

	Prevalence, Mean (SD)			
	Any BPD	BP-I	BP-II	Subthreshold BPD
Lifetime	4.4 (24.3)	1.0 (13.2)	1.1 (10.6)	2.4 (23.3)
12-Month	2.8 (18.9)	0.6 (9.2)	0.8 (9.9)	1.4 (15.1)

Subthreshold BPD is common, clinically significant, and underdetected  
75% of subthreshold BPD lifetime cases received no medication

Merikangas KR, et al. *Arch Gen Psychiatry*. 2007;64:543-552.

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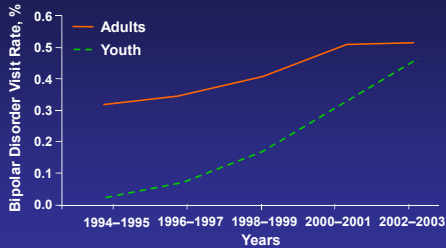
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## National Trends in Increased Outpatient Diagnosis of Bipolar Disorder

Based on the National Ambulatory Medical Care Survey (NAMCS)  
Youth: 0–19 years; Adults: ≥ 20 years



Diagnosis of bipolar disorder for ADULTS increased ~2x in the 10-year study period  
Diagnosis of bipolar disorder for YOUTH increased ~40x in the 10-year study period

Moreno C, et al. *Arch Gen Psychiatry*. 2007;64(9):1032-1039.

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## Criteria for Manic Episode

- A. Requires a period of elevated, expansive, or irritable mood lasting at least 1 week (less if hospitalization is necessary)
- B. Along with 3 or more of the following persistent symptoms (4 if the mood is only irritable):
  1. Grandiosity
  2. Decreased need for sleep
  3. Pressure to keep talking
  4. Flight of ideas or racing thoughts
  5. Distractibility
  6. Psychomotor agitation
  7. Excessive involvement in activities that have high potential for painful consequences
- C. Symptoms do not meet mixed episode criteria
- D. Severe enough to cause impairment
- E. Not due to substance use or medical condition

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*. Washington, DC: American Psychiatric Association; 2000.

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## Diagnostic Features of Depressive Episode

- A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning. At least one of the symptoms is either:
  - 1) Depressed mood
  - OR
  - 2) Loss of interest or pleasure (anhedonia)
  - 3) Appetite/weight changes
  - 4) Insomnia or hypersomnia
  - 5) Reduced energy, fatigue
  - 6) Difficulty with concentration
  - 7) Inappropriate guilt
  - 8) Suicidal preoccupation
  - 9) Psychomotor changes
- B. Symptoms do not meet criteria for a mixed episode
- C. Associated with significant impairment
- D. Symptoms not due to a general medical condition or direct effect of a substance (drug abuse, medication)
- E. Symptoms not accounted for by bereavement

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*. Washington, DC: American Psychiatric Association; 2000.

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## Bipolar I vs Bipolar II

### Bipolar I

- Requires mania for diagnosis
- Mixed states (mania + major depression) occur in 40%
- Highly familial
- Suicide: 10–15% completed
- Comorbid substance abuse in 60%

### Bipolar II

- Recurrent hypomania + major depression
- Female:male = 2:1
- Diagnostic challenges:
  - Hypomania not experienced as "abnormal"
  - Prior hypomania often not reported

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*. Washington, DC: American Psychiatric Association; 2000.

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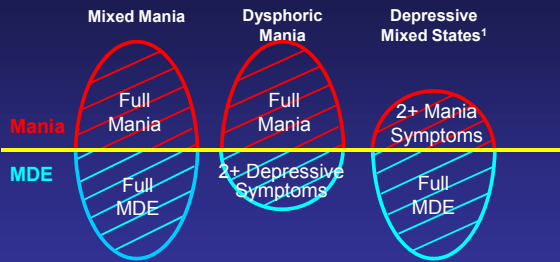
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## Mixtures of Manic and Depressed Symptoms Are Commonly Seen



MDE = major depressive episode

Agitated depressions? <sup>2,3</sup>

1. Benazzi F. *Psychiatry Res*. 2004;127:247-257.
2. Maj M, et al. *Am J Psychiatry*. 2003;160:2134-2140.
3. Akiskal HS, et al. *J Affect Disord*. 2005;85:245-258.

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## All Depressions Are Not the Same!

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## Clues That "Unipolar" Depression May Be Bipolar Depression

- Early age of onset
- Postpartum onset of first major depression
- Seasonal mood changes
- Hypersomnia and/or psychomotor slowing
- Severe anhedonia
- Depression with catatonia and/or psychotic features
- Bipolar family history
- Treatment-emergent mania or hypomania
- History of recurrent but brief depressive episodes

- Merchand WR. *Hosp Physician*. 2003;39:21-30.  
 Geller B, Luby J. *J Am Acad Child Adolesc Psychiatry*. 1997;36:1168-1176.  
 Akiskal HS, et al. *J Affect Disord*. 1983;5:115-128.

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## Characteristics of Increased Vulnerability/Risk for Bipolar Disorder

*Important to consider in association with prodromal symptoms*

- Risk Factors
  - Family history of bipolar disorder, unipolar depression
  - Obstetric complications, winter-spring births, early traumatic brain injury
  - Childhood history of physical/sexual abuse
  - Stressful life events – death of a close relative (especially suicide)
- Markers of Potential Vulnerability
  - Biological markers
    - Abnormal regulation of circadian system
    - Response to sleep deprivation
    - White matter hyperintensities
    - Response to psychostimulants
    - Cholinergic sensitivity
  - Neurodevelopmental features
    - Delayed language, social, motor development
  - Behavioral problems
  - Temperament/Personality factors
    - Dysthymic, cyclothymic, hyperthymic

Conus P, et al. *Bipolar Disord.* 2008;10:555-565.

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## Bipolar Prodrome: Differential Diagnosis

- Major depressive disorder
- Borderline personality disorder
- Agitated depression
- Substance use disorder
- Externalizing behavior disorder

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## Limitations of Operationalizing the Prodrome

Consider Robins & Guze Criteria for Diagnostic Validity in Mental Illness<sup>1</sup>:

1. Phenomenology
2. Family history
3. Course of illness
4. Exclusion criteria/diagnostic boundary (e.g., treatment response/effects, prodromal manifestations)
5. Biological studies

Additional limitations

- Retrospective recognition of prodromal symptoms
- Non-specificity, widespread nature of symptoms, such as anxiety, depression
- Psychiatric comorbidities
- Difficulty in obtaining a complete accounting of symptoms, risk factors, vulnerabilities; need for collateral informants
- Guidelines do not provide treatment recommendations for prodromal patients (prior to first manic episode)

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1. Robins E, Guze S. *Am J Psychiatry.* 1970;126(7):983-987.







## Benefits of Psychotherapeutic Interventions

- Adjustment to diagnosis and treatment
- Enhanced adherence
- Improved self-esteem
- Reduced risky behaviors
- Modification of destabilizing biopsychosocial factors
- Management of stressors
- Learning coping strategies
- Early recognition
- Modification attitudes/beliefs

Scott J, Gutierrez MJ. *Bipolar Disord*. 2004;6:498-503.

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## Economic Burden of Bipolar Disorder

- Direct and Indirect Costs
  - Clinic visits
  - Hospitalizations
  - Drug costs
  - Financial burden on caregivers
  - Functional impairment
  - Missed work hours, lost earnings
  - Reduced productivity
- Delay between onset of illness and diagnosis/treatment  
~8-10 years
  - Increased illness burden
  - Increased cost of care

Kleinman L, et al. *Pharmacoeconomics*. 2003;21(9):601-622.  
Kessler R, et al. *Am J Psychiatry*. 2008;165:703-711.  
Birnbaum H, et al. *J Clin Psychiatry*. 2003;64:1201-1209.

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## Economic Burden of Bipolar Disorder

- Prevalence-based analysis: total annual costs estimated at **\$45.2 billion** (US, 1991 values)
- Incidence-based analysis: lifetime costs estimated at **\$24 billion** (US, 1998 values)
- 2009 Mayo Clinic Study
  - Review of health care claims over a 4 year period
  - Patients with bipolar disorder had significantly higher monthly costs than diabetes, depression, asthma and coronary artery disease
  - Only patients with both coronary artery disease and diabetes had higher costs

Kleinman L, et al. *Pharmacoeconomics*. 2003;21(9):601-622.  
Stimmel G. *Psychiatr Serv*. 2004;55(2):117-118.  
Williams M, et al. APA Annual Meeting May 16-21, 2009 San Francisco, CA. Abstract NR7-062.

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## Barriers

Primary Care Physicians Reporting Difficulty Obtaining Mental Health Services<sup>1</sup>

Type of Practice	Outpatient Mental Health Services (N = 6,319)	Inpatient Mental Health Services (N = 5,933)
Family practice	53%	54%
Pediatrics	60%	64%
General internists, other	50%	46%

2004–2005 Community Tracking Study Physicians Survey (N = 2,900)<sup>2</sup>

- **Two-thirds** unable to get outpatient mental health services for patients (> 2x rate reported for access to other specialists, imaging services, non-emergency hospital admissions)

- Reasons given for not getting services (rated as very important)

- Lack of or inadequate insurance coverage - 59%
- Health plan barriers - 51.1%
- Shortage of providers - 58.9%

1. Trude S, Stoddard J. *J Gen Intern Med*. 2003;18:442-449.  
2. Cunningham P. *Health Affairs*. 2009;28(3):490-501.

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## Summary

- Accurate diagnosis of bipolar disorder is the first step in an effective treatment strategy
  - Distinguish unipolar depression from bipolar depression
  - Consider risk factors for bipolar disorder and symptoms of bipolar prodrome
  - Utilize tools for screening, monitoring response to therapy
- Use clinical principles to select pharmacological and non-pharmacological interventions based on sound rationales and strategies
- Carefully and consistently monitor outcomes, including safety
- The personal and economic burdens associated with bipolar disorder are high; efforts to maximize access to care and services are critical

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## Patient Interview

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## Jill – Present Illness

- Concern regarding panic “attacks”
  - Feels like she can’t breathe
  - Throat is closing up
  - Vision out of focus
  - Chest pain, heart pounding
  - Started several months ago, getting progressively worse

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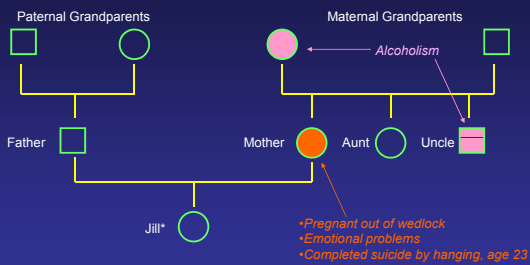
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## Jill’s Genogram



\*Adopted by maternal aunt

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## History

- Social history
  - Associate's degree in marketing; works for local car dealership
  - Divorced, bisexual, currently living with female significant other
  - 1 pack of cigarettes daily; drinks occasionally (intoxicated 3x in last year); prior experimentation with illicit drugs
  - Accomplished singer, self-taught guitarist; performs at local nightclubs

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## History (cont)

- Medical history
  - G<sub>2</sub>P<sub>0</sub>A<sub>2</sub> (1<sup>st</sup> trimester abortions)
  - Pelvic inflammatory disease at age 21 resulting in infertility
  - Total abdominal hysterectomy at age 30

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## History (cont)

- Psychiatric history
  - Prone to extremes of mood
  - Self-described “Eeyore” who becomes “Tigger”
  - Hypomanic periods last 1-3 weeks; more irritability, less expansive or elevated mood
  - No psychiatric hospitalizations
  - Tylenol PM overdose at age 17
  - Benzodiazepine use without prescription
  - Short-term treatment for depression with sertraline a few years ago

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## Patient Health Questionnaire 9 (PHQ-9)

Name: Jill

Date: Visit 1

Over the last 2 weeks, how often have you been bothered by any of the following problems? (use “✓” to indicate your answer)

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself in some way	0	1	2	3
<b>Total</b>			<b>18</b>	
10. If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home or get along with other people	Not difficult at all _____ Somewhat difficult _____ Very difficult _____ Extremely difficult ✓ _____			

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**CIDI Part III. Criterion B Symptom Questions**

Think of an episode when you had the largest number of changes like these at the same time. During that episode, which of the following changes did you experience?

- 1. Were you so irritable that you either started arguments, shouted at people, or hit people? **YES**
- 2. Did you become so restless or fidgety that you paced up and down or couldn't stand still? **YES**
- 3. Did you do anything else that wasn't usual for you – like talking about things you would normally keep private, or acting in ways that you'd usually find embarrassing? **YES**
- 4. Did you try to do things that were impossible to do, like taking on large amounts of work? **YES**

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**CIDI Part III. Criterion B Symptom Questions (cont)**

- 5. Did you constantly keep changing your plans or activities? **YES**
- 6. Did you find it hard to keep your mind on what you were doing? **YES**
- 7. Did your thoughts seem to jump from one thing to another or race through your head so fast you couldn't keep track of them? **YES**
- 8. Did you sleep far less than usual and still not get tired or sleepy? **YES**
- 9. Did you spend so much more money than usual that it caused you to have financial trouble? **YES**

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