SYLLABUS AND COURSE GUIDE

Applying Performance Measures Through a Chronic Disease Model to Optimize Treatment of Bipolar Mania



A Free, One-Hour CME/CNE/CEP/NASW/CCMC/CPE Live and On Demand Activity

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FACULTY: Leslie Citrome, MD, MPH, and Gary S. Sachs, MD **MODERATOR:** Roger S. McIntyre, MD, FRCPC

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INFORMATION FOR PARTICIPANTS

Statement of Need

Bipolar disorder is a complicated and severe mental disorder associated with a recurrent or chronic course, insufficient clinical response, and psychosocial impairment in a substantial number of patients. Bipolar disorder presents with pleomorphic signs and symptoms varying from depression to hypomania, full-blown mania, mixed states, and psychosis. Due to the complexity of the disease, the assessment of patients with bipolar disorder poses a difficult challenge to clinicians. Upon diagnosis, it is paramount to understand the different classifications of medications available for treatment to ensure the patient is getting the best care possible based on evidence and treatment guidelines considering safety and long-term efficacy. In this neuroscienceCME Live and On Demand activity, the faculty will apply a chronic disease model to the diagnosis and management of bipolar mania focusing on achievement of performance measure-based benchmarks that can improve patient outcomes.

Bauer MS, et al. Enhancing multiyear guideline concordance for bipolar disorder through collaborative care. *Am J Psychiatry* 2009;166:1244-1250. Kupfer DJ, et al. Demographic and clinical characteristics of individuals in a bipolar disorder case registry. *J Clin Psychiatry* 2002;63:120–125.

Activity Goal

To improve utilization of measurement tools within a chronic disease model in patients with bipolar mania.

Learning Objectives

At the end of this CE activity, participants should be able to:

- Identify strategies for detecting mania or hypomania in patients presenting with depressive symptoms, in accordance with validated guidelines and performance measures.
- Compare evidence-based treatment strategies that can be implemented early in the course of bipolar disorder to address mania symptoms.
- Recognize the elements of a chronic care model that should be considered when developing a long-term management plan in patients with bipolar mania.

Target Audience

Physicians, physician assistants, nurse practitioners, nurses, psychologists, social workers, certified case managers, pharmacists, and other healthcare professionals interested in mental health.

CREDIT INFORMATION

CME Credit (Physicians)

Indiana University School of Medicine is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. Indiana University School of Medicine designates this educational activity for a maximum of 1.0 AMA PRA Category 1 Credit(s) $^{\text{TM}}$. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Note to Physician Assistants: AAPA accepts Category I credit from AOACCME, Prescribed credit from AAFP, and AMA Category I CME credit for the PRA from organizations accredited by ACCME.

CNE Credit (Nurses)

This continuing nursing education activity was approved by the New York State Nurses Association, an accredited approver by the American Nurses Credentialing Center's Commission on Accreditation.

It has been assigned approval code 7ZMRM6-10. 1.0 contact hours will be awarded upon successful completion.

CEP Credit (Psychologists)

CME Outfitters is approved by the American Psychological Association to sponsor continuing education for psychologists. CME Outfitters maintains responsibility for this program and its content. (1.0 CE credits)

NASW Credit (Social Workers)

This program was approved by the National Association of Social Workers (provider #886407722) for 1 continuing education contact hour.

CCMC Credit (Certified Case Managers)

This program has been approved for 1 hour by the Commission for Case Manager Certification (CCMC).

CPE Credit (Pharmacists)



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🖳 Universal Program Number: 376-999-10-002-H01-P

Activity Type: knowledge-based

All other clinicians will either receive a CME Attendance Certificate or may choose any of the types of CE credit being offered.

Acknowledgement of Financial Support

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Successful completion of this CE activity includes participating in the live or recorded activity, reviewing the course materials, and following the instructions below by February 17, 2011:

To complete your credit request form, activity evaluation, and post-test online, and print your certificate or statement of credit immediately (70% pass rate required), please visit www.neuroscienceCME.com and click on the Testing/Certification link under the Activities tab (requires free account activation).

There is no fee for participation in this activity. The estimated time for completion is 60 minutes. Questions? Please call **877.CME.PROS**.

FACULTY BIOS & DISCLOSURES

Roger S. McIntyre, MD, FRCPC (Moderator)

Dr. McIntyre is currently an Associate Professor of Psychiatry and Pharmacology at the University of Toronto and Head of the Mood Disorders Psychopharmacology Unit at the University Health Network, Toronto, Canada.

Dr. McIntyre is involved in multiple research endeavours that primarily aim to characterize the association between mood disorders and medical comorbidity. This research involves elucidating metabolic adverse events associated with the use of psychotropic medications, the impact of medical comorbidity on the course of mood disorders, and the effect of glucose homeostasis on neurocognition.

Dr. McIntyre is extensively involved in medical education. He is a highly sought-after speaker at both national and international meetings. He has received several teaching awards from the University of Toronto, Department of Psychiatry and has been a recipient of the joint Canadian Psychiatric Association (CPA)/Council of Psychiatric Continuing Education Award for the Most Outstanding Continuing Education Activity in Psychiatry in Canada.

Dr. McIntyre is a contributor to the CPA guidelines for the treatment of depressive disorders and the Canadian Network for Mood and Anxiety Treatments (CANMAT) guidelines for the management of bipolar disorder. Dr. McIntyre has published extensively in leading peer-reviewed journals and textbooks. Dr. McIntyre is also a reviewer for many journals including the *American Journal of Psychiatry, Biological Psychiatry, Journal of Clinical Psychiatry,* and *The New England Journal of Medicine*.

Dr. McIntyre completed his medical degree at Dalhousie University. He received his Psychiatry residency training and Fellowship in Psychiatric Pharmacology at the University of Toronto.

Leslie Citrome, MD, MPH

Dr. Citrome is Director of the 24-bed inpatient Clinical Research and Evaluation Facility at the Nathan S. Kline Institute for Psychiatric Research in Orangeburg, New York, and Professor of Psychiatry at the New York University School of Medicine. He is a 1983 graduate of the McGill University Faculty of Medicine and in 1987 completed a Residency and Chief Residency in Psychiatry at the New York University School of Medicine. After serving as Clinical Director of Middletown Psychiatric Center, Dr. Citrome joined the Nathan S. Kline Institute for Psychiatric Research in 1994. He received a Masters in Public Health from the Columbia University School of Public Health in 1996. Dr. Citrome is involved as Principal Investigator, Co-Investigator, and Collaborator on a number of ongoing projects centering on psychopharmacologic approaches to schizophrenia, including new and novel

Applying Performance Measures Through a Chronic Disease Model to Optimize Treatment of Bipolar Mania

medications, management of treatment refractory schizophrenia, and the management of aggressive and violent behavior. He is also an active member of the Medication Utilization and Outcomes Research Program that focuses on the practice of psychiatry within the 16 hospitals operated by the New York State Office of Mental Health. He is the author or co-author of over 350 research reports, reviews, and abstracts in the scientific literature, and has lectured extensively throughout the USA, Canada, Europe, and Asia. He is the section editor for Psychiatry for the *International Journal of Clinical Practice*, has served as a guest editor for special issues of *Psychiatric Annals* and the *Journal of Psychopharmacology*, and is a peer reviewer for over 50 journals.

Gary S. Sachs, MD

Dr. Sachs is currently an Associate Professor in Psychiatry at Harvard Medical School and Co-Director of the Bipolar Clinic and Research Program at Massachusetts General Hospital. He is also the Founder of Concordant Rater Systems.

Dr. Sachs earned his medical degree at the University of Maryland School Of Medicine. He interned in family practice and psychiatry at University of Maryland Hospital in Baltimore, was a resident in psychiatry and Chief Resident, Acute Psychiatry Service, at Massachusetts General Hospital in Boston.

Dr. Sachs was Principal Investigator of the NIMH Systematic Treatment Enhancement Program for Bipolar disorder and is a Distinguished Fellow of the American Psychiatric Association. He chairs the Scientific Advisory Committee of the National Alliance on Mental Illness and serves on the scientific advisory board of the Depression and Bipolar Support Alliance. Dr. Sachs is Coeditor-in-chief of *Clinical Approaches to Bipolar Disorder* and serves on numerous editorial boards. Dr. Sachs has authored over 150 articles, abstracts, books, reviews, and book chapters. He currently focuses his work on clinical trial methodology, innovative approaches to clinical practice and patient-centered research.

Amit Anand, MD (Content/Peer Reviewer)

Professor Anand is Professor of Psychiatry and Radiology at Indiana University. Dr. Anand's career for the past 20 years has been dedicated to the finding the cause of psychiatric illnesses, in particular the mood disorders—bipolar disorder and depression. Using a variety of biological and imaging techniques my aim is to discover the cause of these illnesses and how to develop new pharmacological and non-pharmacological treatments for these important illnesses.

Undergraduate: All India Institute of Medical Sciences

Fellowship: Yale University School of Medicine

Board Certifications/Certifications: Diplomate, American Board of Psychiatry and Neurology; Board Certified, American Board of Psychiatry and Neurology; Board Certified, Royal Australian and New Zealand College of Psychiatrists

Current Academic Interests

Teaching: Psychiatric interview techniques, formulation, state-of-the-art treatments for mood disorder and latest research in this area

Clinical: Pharmacological and non-pharmacological treatments of depression and bipolar disorder, novel therapeutics, increased understanding of illness

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Dr. McIntyre has disclosed that he receives grants/research support from Eli Lilly and Company, Janssen-Ortho, Inc., and Shire Pharmaceuticals, as well as Private Industries or Non-Profit Funds: Stanley Medical Research Institute, National Alliance for Research on Schizophrenia and Depression (NARSAD). He serves on the advisory boards of AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, France Foundation, GlaxoSmithKline, Janssen-Ortho, Inc., Solvay/Wyeth, Eli Lilly and Company, Organon, H. Lundbeck A/S, Biovail Pharmaceuticals, Inc., Pfizer Inc., Shire Pharmaceuticals, and Schering-Plough Corporation. He serves on the speakers bureaus of Janssen-Ortho, Inc., AstraZeneca Pharmaceuticals LP, Eli Lilly and Company, H. Lundbeck A/S, Biovail Pharmaceuticals, Inc., Wyeth Pharmaceuticals, and Schering-Plough Corporation.

Dr. Citrome has disclosed that he recieves payments to institution for research from AstraZeneca Pharmaceuticals LP, Lilly USA, LLC, Pfizer Inc., and Janssen, L.P. He serves on the speakers bureaus of AstraZeneca Pharmaceuticals LP, Lilly USA, LLC, Merck & Co.,

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Inc., and Pfizer Inc. He serves as a consultant to Lilly USA, LLC, GlaxoSmithKline, Janssen, L.P., Merck & Co., Inc., and Pfizer Inc.

Dr. Sachs has disclosed that he receives grant support from GlaxoSmithKline, National Institute of Mental Health, and Repligen Corporation. He serves as a consultant to, or on the advisory boards of, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Cephalon, Inc., Concordant Rater Systems, Eli Lilly and Company, GlaxoSmithKline, Janssen, L.P., Merck & Co., Inc., Otsuka America Pharmaceutical, Inc., Pfizer Inc., Schering-Plough Corporation, Sepracor Inc., Repligen Corporation, Sanofi-aventis, and Wyeth Pharmaceuticals.

Dr. Anand has disclosed that he has received honoraria from Pfizer Inc. as a consultant, and has received research grants from Eli Lilly and Company and AstraZeneca Pharmaceuticals LP as an independent investigator.

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Activity Slides

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Abbreviation List

AED Antiepileptic drug

ARI Aripiprazole

ASE Asenapine

CBZ-ER Carbamazepine extended release

CIDI Composite International Diagnostic Interview

DSM Diagnostic and Statistical Manual of Mental Disorders

DVP Divalproex

FDA Food & Drug Administration

MADRS Montgomery-Asberg Depression Rating Scale

MDD Major depressive disorder

MDQ Mood Disorders Questionnaire

MINI Mini International Neuropsychiatric Interview

NOS Not otherwise specified

OLZ Olanzapine

PBO Placebo

QUE Quetiapine

RCT Randomized controlled trial

RIS Risperidone

SCID Structured Clinical Interview for DSM-IV Disorders

SRF-ME Self-Report Form for Mood Episodes

STABLE STAndards for BipoLar Excellence

STEP-BD Systemic Treatment Enhancement Program for Bipolar Disorder

WFSBP World Federation of Societies of Biological Psychiatry

YMRS Young Mania Rating Scale

ZIP Ziprasidone

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Moderator: Roger S. McIntyre, MD, FRCPC

Head, Mood Disorders
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Toronto, ON

Roger	S.	McIntyre,	MD,	FRCPC
_		Disclosure	95	

- Research/Grants: Eli Lilly and Company; Janssen-Ortho, Inc.; Shire Pharmaceuticals; Private Industries or Non-Profit Funds: Stanley Medical Research Institute; National Alliance for Research on Schizophrenia and Depression (NARSAD)
- Speakers Bureau: AstraZeneca Pharmaceuticals LP; Biovail Pharmaceuticals, Inc.; Eli Lilly and Company; Janssen-Ortho, Inc.; H. Lundbeck A/S; Schering-Plough Corporation; Wyeth Pharmaceuticals
- Consultant: None
- Stockholder: None
- Other Financial Interest: None
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- Stockholder: None
- Other Financial Interest: None
- Advisory Board: None

Gary	S.	Sachs,	MD
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Co-Director, Bipolar Clinic and Research Program Massachusetts General Hospital Founder, Concordant Rater Systems Associate Professor of Psychiatry Harvard Medical School Boston, MA

Gary	S.	Sachs	, MD
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- Research/Grants: GlaxoSmithKline; National Institute of Mental Health; Repligen Corporation
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- Stockholder: None
- Other Financial Interest: None



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February 17, 2010

Supported by educational grants from Bristol-Myers Squibb Company and Otsuka America Pharmaceutical, Inc., and from Pfizer Inc.

Learning **1** Objective

Identify strategies for detecting mania or hypomania in patients presenting with depressive symptoms, in accordance with validated guidelines and performance measures

Learning **2** Objective

Compare evidence-based treatment strategies that can be implemented early in the course of bipolar disorder to address mania symptoms

Learning 3 Objective

Recognize the elements of a chronic care model that should be considered when developing a long-term management plan in patients with bipolar mania

Learning **1** Objective

Identify strategies for detecting mania or hypomania in patients presenting with depressive symptoms, in accordance with validated guidelines and performance measures

Clinical Guidelines and Performance Measures

- WFSBP guidelines
 - http://www.wfsbp.org/treatmentguidelines/bipolar-disorders.html
- STABLE performance measures
 - http://www.cqaimh.org/stable.html

Bipolar Performance Measures STABLE* Project

- STAndards for BipoLar Excellence organized in 20051
- Develop and test evidence-based measures related to identifying, assessing, managing, and coordinating care for bipolar disorder²
- 5 STABLE measures endorsed by National Quality Forum³
 - Screening for mania/hypomania in patients diagnosed with depression Assessment for risk of suicide

 - Assessment for substance use
 Screening for hyperglycemia if atypical antipsychotic agents are prescribed
 Monitoring change in functioning in response to treatment
- * AstraZeneca LP provided financial support for the STABLE Project
- Goldman WE, et al. *J Psychiatr Pract* 2008;Suppl 2:18-30.
 Center for Quality Assessment and Improvement in Mental Health. http://www.cqaimh.org/stable_measures.html.
 National Quality Forum. http://www.qualityforum.org.



GS Presentation

Age: 28 Gender: Female

Occupation: IT professional

- Your history with GS
 - GS is an established patient you have managed for 2 years for the diagnosis of major depressive disorder (MDD) with recurrent episodes
 - Conventional antidepressant therapy has been modestly effective with no sustained benefit and has been often poorly tolerated
 - She has also received cognitive behavioral therapy with little benefit
- Complaint today
 - "That last antidepressant you started me on 3 weeks ago is not helping me one bit."

GS Key Interview Dialogue

- Dr: Why do you feel that the medication is not working?
- GS: My depression is worse and my work is starting to
- Dr: In what way is your depression worse?
- I am less tired, but I am nervous and anxious. The nervousness causes me to lose focus on what I'm doing. When this happens at work, I don't get anything done. I am also particularly irritated with my boyfriend, lately. I snap at him. All this has my self-esteem in the toilet.
- Dr: How have you been sleeping? How many hours a night?
- Only about 3 or 4. Like I already said to you, I am LESS TIRED. Aren't you listening to me?

Internet Poll #1

Would you change the working diagnosis for GS?

- A. No. She still has unipolar depression (MDD).
- B. Yes. She has bipolar disorder.
- C. Yes. She has schizophrenia.

Summary of DSM-IV Criteria for Mania

Predominant	Duration Symptom	Associated
Mood State	Threshold	Features
High, happy, euphoric, expansive, irritable	At least 1 week, with 3 symptoms present to a significant degree or any duration if hospitalized Marked impairment of social or occupational function	

Sachs G. FOCUS 2007;5:3-13.

Summary of DSM-IV Criteria for Hypomania

Predominant	Duration Symptom	Associated
Mood State	Threshold	Features
High, happy, euphoric, expansive, irritable	At least 4 days with 3 symptoms present to a significant degree	Increased self-esteem/ grandiosity Decreased need for sleep More talkative Racing thought/ flight of ideas Distractible Increased goal-directed activities/psychomotor agitation Risk-taking (potential painful consequences)

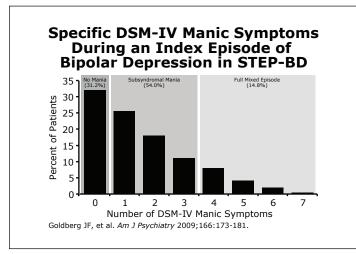
Sachs G. FOCUS 2007;5:3-13.

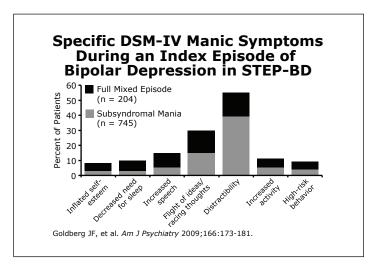
Manic Episodes Are Less Common, But Critical to Recognize

- Symptomatic bipolar disorder patients spend, on average, 33% of their time in a depressive phase compared with 11% in a manic/hypomanic phase¹
- Patients generally do not recognize or spontaneously report prior hypomania as they view these periods as normal happiness or well-being²

1.	Post RM,	et al.	Exp Rev	Neurother	2004;6(Supp	l 2):S27-S33
2	Dorle M	a+ al /	Dinalar D	icard 200E	.7.11 71	

2. Berk M, et al. *Bipolar Disord* 2005:7;11-21.

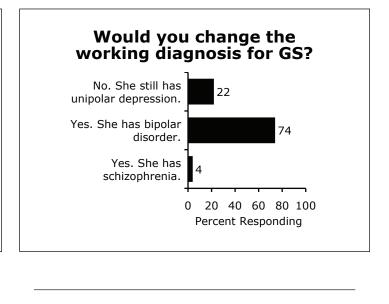




Presence of Mania Changes the Diagnosis

Disorder	Depressive Episode	Manic or Mixed Episode	Hypomanic Episodes
Bipolar I Disorder	Common but not required	≥ 1 required	Common but not required
Bipolar II Disorder	≥ 1 required	None allowed	≥ 1 required
Bipolar Disorder NOS*	Common but not required	None allowed	Not required
Cyclothymic Disorder	Dysthymia, but not major depression	None allowed	Numerous periods over 2 years required
Major Depressive Disorder	≥ 1 required	None allowed	None allowed
Dysthymic Disorder	Dysthymic Disorder ≥ 2 years required but not major depression		None allowed

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



Diagnostic Challenges

- Depression is a common chief complaint during manic episodes
- · Vague diagnostic criteria
- Poor documentation of prior history
- Diagnostic criteria overemphasize episode characteristics
- Mixed episodes
- Current affective state influences perceptions and reporting
- Absence of collateral informants
- · Comorbid conditions are common
- Lack of validated biological markers
- Longitudinal factors

Sachs G. FOCUS 2007;5:3-13.

Bipolar Mixed States Are Often "Missed States"

- Bipolar mixed states
 - Depression and mania co-occurring¹
- Depressive mixed states
 - Core of depression, but with racing thoughts¹
- Dysphoric mania common especially in women²
- Mixed hypomania²

1.	Berk M,	et al. Aust N Z Psych 2005;39:215-221.	
2	Sunnes	T et al Arch Gen Psychiatry 2005:62:1089-1096	

Hazards of Misdiagnosis

Inaccurate or delayed diagnosis of bipolar disorder increases risk of:

- Rapid cycling or mixed features
- Suicide attempts or completion
- Violent behavior; impulsive behavior
- Sexual and other indiscretions
- Worsening substance abuse
- Loss of job or significant other
- Treatment resistance

Assessment Tools

- Screening
 - Mood Disorders Questionnaire (MDQ)*
- Diagnosis
 - Structured Clinical Interview for DSM-IV Disorders (SCID)
 - Composite International Diagnostic Interview (CIDI)
- Monitoring
 - Young Mania Rating Scale (YMRS)*
 - Montgomery-Åsberg Depression Rating Scale (MADRS)*
 - Self-Report Scale
 - Self-Report Form for Mood Episodes (SRF-ME)
- * Additional information and/or downloads available at www.neursocienceCME.com.

Mood Disorder Questionnaire (MDQ)

- Designed for screening
- 15 items
- Self-assessment questionnaire
- Can be completed and scored in < 5 minutes

Hirschfeld RMA. J Clin Psychiatry Prim Care Companion 2002;4:9-11.

Mood Disorder Questionnaire (MDQ)

- Hyper or more energetic than usual
- Predominantly or thematically irritable
- Distinctly self-confident, positive, or self-assured
- Less sleep than usual
- More talkative or speaking faster than usual
- · Racing thoughts
- Easily distracted
- Problems at work and socially
- More interest in sex
- Taking unusual risks
- Excessive spending

Hirschfeld RMA, et al. *Am J Psychiatry* 2000;157:1873-1875. Hirschfeld RMA. *J Clin Psychiatry Prim Care Companion* 2002;4:9-11.

Diagno	ostic	Conf	idence
The I	Bipola	rity 1	Index

- Continuous measure of diagnostic confidence
- Complements tools for DSM categorical diagnosis
 - MIŇI and SCID
- Multidimensional clinical diagnosis of bipolar disorder
 - 5 dimensions
 - Subject compared to classic conception of bipolar disorder

Sachs GS. Acta Psychiatr Scand Suppl 2004;110:7-17.

Learning 2 Objective

Compare evidence-based treatment strategies that can be implemented early in the course of bipolar disorder to address mania symptoms

Internet Poll #2

How would you treat GS?

- A. Optimize current regimen
- B. Switch to lithium
- C. Switch to an atypical antipsychotic
- D. Add atypical antipsychotic to current regimen

Agents with Highest and Lowest Evidence Category for Acute Mania WFSBP Guidelines

Grunze H, et al. World J Biol Psychiatry 2009;10:85-116.

Category A Positive

- Lithium
- Valproate
- Carbamazepine
- Haloperidol .
- Olanzapine
- Risperidone
- Quetiapine
- Ziprasidone
- Aripiprazole
- Asenapine
- Category A = superiority to PBO \geq 2 RCTs; Category E = non-superiority to PBO; Category F = efficacy or non-efficacy not proven

Category E or F Negative or Failed

- Gabapentin
- Lamotrigine
- Pregabalin
- Tiagabine
- Topiramate

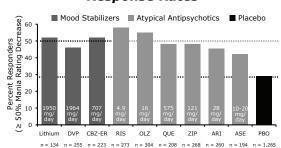
FDA-Approved Oral Agents for Adults with Bipolar Disorder

Generic Name	Manic	Mixed	Maintenance	Depression
Valproate	Х			
Carbamazepine extended release	х	х		
Lamotrigine			Х	
Lithium	Х	Х	Х	
Aripiprazole	Х	Х	Х	
Ziprasidone	Х	Х	X*	
Risperidone	Х	Х		
Asenapine	Х	Х		
Quetiapine	Х	Х	X*	Х
Chlorpromazine	Х			
Olanzapine	Х	Х	Х	
Olanzapine/fluoxetine combination				х

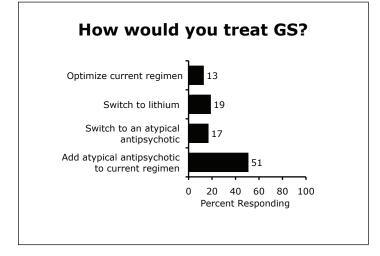
^{*} Augmentation only

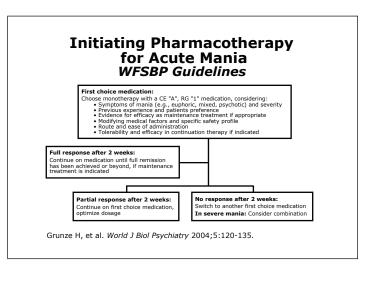
Drugs@FDA. Available at http://www.accessdata.fda.gov/Scripts/cder/DrugsatFDA. Accessed October 22, 2009.

Acute Mania Monotherapy Studies Response Rates



Adapted from Ketter TA (ed). Advances in the Treatment of Bipolar Disorders. Am Psychiatric Press, Inc. 2005:13. McIntyre RS, et al. *Bipolar Disord* 2009;11:673-686.





Areas of Concern with Agents Used to Treat Bipolar Disorder

- Lithium

 - Weight gain
 Teratogenic
 Thyroid dysfunction
- Antiepileptic drugs (AEDs)
 Weight gain
 Sedation

 - Teratogenic
 Increased risk of suicidal ideation/suicide
 Cognitive impact
- Atypical antipsychotics
 Weight gain
 High fasting glucose
 Increase in prolactin

 - Sedation
 - ActivationExtrapyramidal symptoms

Drugs@FDA. Available at http://www.accessdata.fda.gov/Scripts/cder/DrugsatFDA. Accessed October 22, 2009.

Adverse Events Associated with Atypical Antipsychotics

Adverse Event	Clozapine	Olanzapine	Risperidone	Quetiapine	Ziprasidone	Aripiprazole
Metabolic						
Weight gain	++++	+++	++	++	+/0	+/0
Dyslipidemia	++	+++	+	+	0	0
Glucose dysregulation	++	++	+	+	0	0
Neurological						
Somnolence/sedation	++++	+++	++	+++	+	+
Extrapyramidal Symptoms	0	+	++	0	+	+
Cardiovascular						
Myocarditis / Cardiomyopathy	+/0	0	0	0	0	0
QTc prolongation	+/0	+/0	+/0	+	+	0
Hormonal						
Prolactin	0	+/0	++	0	0	0

Number of "+" symbols signifies extent of adverse event; 0 = neutralMcIntyre RS, Konarski JZ. J Clin Psychiatry 2005;66:28-36.

Learning 3 Objective

Recognize the elements of a chronic care model that should be considered when developing a long-term management plan in patients with bipolar mania

Key Components of "Best Practice" Chronic Care Delivery

- Patient-centered
 - Focus on patient self-care
- Longitudinal
- Collaborative
- Multidisciplinary

Management F	rior	ity	Based	on
Concordance	and	Ad	heren	ce

	Concordant	Discordant		
Adherent	Maintain concordance by recognition of collaborative therapeutic outcomes	Improve concordance by recognition of self interest and options for improved therapeutic outcomes		
Nonadherent	Build external supports	Establish therapeutic alliance; Clarify areas of agreement; Recognize outcomes in the absence of collaborations		

Chronic Care for Bipolar Mania Must Focus on Adherence

- A significant problem
- Getting patient buy-in will improve adherence with the treatment plan
- Carefully assess nonresponders for nonadherence

Clinical Connections

- Bipolar disorder
 - Is often misdiagnosed as depression due to the prevalence of depressive episodes often as the presenting phase
 - Can masquerade in different or mixed mood states
- Misdiagnosis can have serious detrimental effects on treatment effectiveness and outcomes
- Use therapeutic modalities with the highest level evidence to manage manic episodes

Clinical Connections

- Counsel patients on benefits and side effects of therapy
- Improved patient outcomes can be achieved by:
 - Providing care as part of a collaborative healthcare team
 - Forming an alliance with the patient (i.e., get their buy-in)
 - Being alert to possible patient nonadherence



Bibliography

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

Berk M, Dodd S, Malhi GS. 'Bipolar missed states': the diagnosis and clinical salience of bipolar mixed states. *Aust N Z J Psych* 2005;39:215-221.

Berk M, Dodd S. Bipolar II disorder: a review. Bipolar Disord 2005;7:11-21.

Center for Quality Assessment and Improvement in Mental Health. Available at: http://www.cqaimh.org/stable_measures.html.

Drugs@FDA. Available at: http://www.accessdata.fda.gov/Scripts/cder/. DrugsatFDA. Accessed October 22, 2009.

Goldberg JF, Perlis RH, Bowden CL, et al. Manic symptoms during depressive episodes in 1,380 patients with bipolar disorder: findings from the STEP-BD. *Am J Psychiatry* 2009;166:173-181.

Goldman WE, Hermann RC, Jewell M, Brewster C. Development of evidence-based performance measures for bipolar disorder: overview of methodology. *J Psychiatr Pract* 2008;14(Suppl 2):18-30.

Grunze H, Kasper S, Goodwin G, Bowden C, Moller HJ; WFSBP Task Force on Treatment Guidelines for Bipolar Disorders. The World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the biological treatment of bipolar disorders, part III: maintenance treatment. *World J Biol Psychiatry* 2004;5:120-135.

Grunze H, Vieta E, Goodwin GM, et al. The World Federation of Societies of Biological Psychiatry (WSFBP) guidelines for the biological treatment of bipolar disorders: update 2009 on the treatment of acute mania. *World J Biol Psychiatry* 2009;10:85-116.

Hirschfeld RM, Williams JB, Spitzer RL, et al. Development and validation of a screening instrument for bipolar spectrum disorder: the Mood Disorder Questionnaire. *Am J Psychiatry* 2000;157:1873-1875.

Hirschfeld RM. The Mood Disorder Questionnaire: a simple, patient-rated screening instrument for bipolar disorder. *Prim Care Companion J Clin Psychiatry* 2002;4:9-11.

Ketter TA, ed. Advances in the Treatment of Bipolar Disorders. Washington, DC: American Psychiatric Press, Inc.; 2005, 13.

McIntyre RS, Cohen M, Zhao J, Alphs L, Macek TA, Panagides J. A 3-week, randomized, placebo-controlled trial of asenapine in the treatment of acute mania in bipolar mania and mixed states. *Bipolar Disord* 2009;11:673-686.

McIntyre RS, Konarski JZ. Tolerability profiles of atypical antipsychotics in the treatment of bipolar disorder. *J Clin Psychiatry* 2005;66(Suppl 3):28-36.

National Quality Forum. Available at: http://www.gualityforum.org.

Post RM, Calabrese JR. Bipolar depression: the role of atypical antipsychotics. Expert Rev Neurother 2004;4(Suppl 2):S27-S33.

Sachs GS. Bipolar disorder clinical synthesis: where does the evidence lead? Focus 2007;5:3-13.

Sachs GS. Strategies for improving treatment of bipolar disorder: integration of measurement and management. *Acta Psychiatr Scand Suppl* 2004;(422):7-17.

Suppes T, Mintz J, McElroy SL, et al. Mixed hypomania in 908 patients with bipolar disorder evaluated prospectively in the Stanley Foundation Bipolar Treatment Network: a sex-specific phenomenon. *Arch Gen Psychiatry* 2005;62:1089-1096.