BRINGING BIPOLAR I TO LIGHT

CONNECTING ON DIAGNOSIS AND TREATMENT CHALLENGES

ADDITIONAL RESOURCES

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Bipolar I disorder can be challenging to diagnose and treat. To address these challenges, three faculty experts came together during Mental Illness Awareness Week to discuss key issues in bipolar I disorder care. In this 60-minute activity previously aired as a live broadcast, the faculty discuss how you can overcome challenges in diagnosis and treatment adherence. Further, they utilize lecture, discussion, and debate to help you individualize treatment and discuss long-acting injectable (LAI) antipsychotics based on the evidence.

Activity Agenda

1 Welcome and Session Overview

2 Panel Discussion:
Overcoming Diagnostic Challenges for Bipolar I Disorder
Moderator: Dr. McIntyre
Panelists: Dr. Becher-Smith and Dr. Goldberg

3 Presentation:
Managing Bipolar I Disorder—Individualizing Treatment Based on the Evidence
Dr. Goldberg

4 Question and Answer Session

5 Clinical Topic Debate:
Atypical LAI Antipsychotics for Bipolar I Disorder—To Use or Not to Use (Based on the Evidence)
Moderator: Dr. Becher-Smith
Debaters: Dr. Goldberg and Dr. McIntyre

6 Panel Discussion:
Overcoming Challenges in Treatment Adherence in Patients With Bipolar I Disorder
Moderator: Dr. Becher-Smith
Panelists: Dr. Goldberg and Dr. McIntyre

7 Question and Answer Session

8 Closing Remarks

Note: This activity is a recording of a previously aired broadcast.

Learning Objectives

Upon completion of this activity, participants should increase their ability to

- Diagnose bipolar I disorder earlier in patients.
- Discuss LAI antipsychotics as a treatment option for appropriate patients with bipolar I disorder.
- Develop individual, evidence-based management plans for patients with bipolar I disorder.
- Implement the latest strategies to improve patient adherence to bipolar I disorder treatment regimens.

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Faculty Presenter Biographies

ROGER S. MCINTYRE, MD, FRCPC

Professor of Psychiatry and Pharmacology, University of Toronto
Head, Mood Disorders Psychopharmacology Unit
Chairman and Executive Director, Brain and Cognition Discovery Foundation
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Roger S. McIntyre, MD, FRCPC, is Professor of Psychiatry and Pharmacology at the University of Toronto and Head of the Mood Disorders Psychopharmacology Unit at University Health Network in Toronto, Ontario, Canada, where he is also Chairman and Executive Director of the Brain and Cognition Discovery Foundation. Additionally, he serves as Director and Co-Chair of the Scientific Advisory Board of the Depression and Bipolar Support Alliance in Chicago, Illinois; Professor and Nanshan Scholar at Guangzhou Medical University in China; Adjunct Professor at the Korea University College of Medicine in Seoul; Clinical Professor at the SUNY Upstate Medical University in Syracuse; and Clinical Professor in the Department of Psychiatry and Neurosciences at the University of California, Riverside School of Medicine. Dr. McIntyre was named one of The World's Most Influential Scientific Minds by Clarivate Analytics in 2014, 2015, 2016, 2017, 2018, and 2019. This distinction is given by publishing the largest number of articles that rank among those most frequently cited by researchers globally in 21 broad fields of science and social science during the previous decade. Dr McIntyre is also the President and CEO of Champignon.

Dr. McIntyre is involved in multiple research endeavors, which primarily aim to characterize the association between mood disorders, notably cognitive function and medical comorbidity. His work broadly aims to characterize the underlying causes of cognitive impairment in individuals with mood disorders and their impact on workplace functioning. This body of work has provided a platform for identifying novel molecular targets to treat and prevent mood disorders and accompanying cognitive impairment.

Dr. McIntyre is extensively involved in medical education, and 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/Council of Psychiatric Continuing Education Award for the Most Outstanding Continuing Education Activity in Psychiatry in Canada.

Dr. McIntyre is the lead author for the *Florida Best Practice Psychotherapeutic Medication Guidelines for Adults With Major Depressive Disorder and Bipolar Disorder*. He is also a contributor to the CANMAT guidelines for the treatment of depressive disorders and bipolar disorders, and he has published more than 600 articles/manuscripts and has edited or co-edited several textbooks on mood disorders.

Dr. McIntyre received his medical degree from Dalhousie University in Halifax, Nova Scotia, Canada. He completed a residency in Psychiatry and a fellowship in Psychiatric Pharmacology at the University of Toronto.

Faculty Presenter Biographies (cont.)

AMY BECHER-SMITH, DNP, MSW, PMHNP, FNP

Assistant Professor of Clinical Practice,
The Ohio State University College of Nursing
Columbus, Ohio

Amy Becher-Smith, DNP, MSW, PMHNP, FNP, is Assistant Professor of Clinical Practice at The Ohio State University College of Nursing in Columbus. She received her Doctor of Nursing Practice degree from The Ohio State University. Dr. Becher-Smith is dually certified in Psychiatry and Family Medicine. She has dedicated her career to working with vulnerable and under-served populations, specifically individuals with serious mental illness, including bipolar I disorder and substance use disorders, and survivors of trauma. Dr. Becher-Smith is dedicated to the implementation of evidence-based practice into treatment to promote healthy outcomes in clients, families, and the community.

JOSEPH F. GOLDBERG, MD, MS

Clinical Professor,
Psychiatry Icahn School of Medicine at Mount Sinai
New York, New York

Joseph F. Goldberg, MD, MS, is Clinical Professor of Psychiatry at the Icahn School of Medicine at Mount Sinai in New York. Dr. Goldberg received his Master of Science in Biological Sciences (concentration in Neuroscience) from the University of Illinois and his medical degree from Northwestern University in Chicago, Illinois. He completed a residency in Psychiatry and a research fellowship in Psychopharmacology Research at the Payne Whitney Psychiatric Clinic at New York-Presbyterian Hospital in New York, New York.

While serving on the faculty at Weill-Cornell Medical Center, Dr. Goldberg was site principal investigator for the National Institute of Mental Health (NIMH) STEP-BD program. His research has focused on the clinical psychopharmacology of bipolar and other mood and psychotic disorders. Dr. Goldberg has received funding from NIMH, the National Alliance for Research on Schizophrenia & Depression, the American Foundation for Suicide Prevention, the Stanley Bipolar Research Foundation and industry, and he is the author of more than 200 peer-reviewed publications and four books, most recently, *Practical Psychopharmacology: Translating Findings from Evidence-based Trials Into Real-world Clinical Practice*, published by Cambridge University Press in 2020. He serves on the Board of Directors for the American Society of Clinical Psychopharmacology, is a Distinguished Fellow of the American Psychiatric Association, and for many years has been named one of America's Top Doctors by Castle Connolly.

Target Audience

This activity is designed for psychiatrists, psychiatric/mental health nurse practitioners (NPs) and physician assistants (PAs), and other healthcare professionals (HCPs) who treat patients with bipolar I disorder.

Accreditation and Credit Designation Statement

Forefront Collaborative is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Forefront Collaborative designates this enduring activity for a maximum of 1.0 *AMA PRA Category 1 Credits*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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The following individuals have indicated that neither they nor their spouses/partners have had, in the past 12 months, financial relationship(s) with commercial interests relative to the content of this CME activity:

- **Planners (Forefront Collaborative):** Leah Johnson and Valerie Siclari, PhD
- **Faculty Presenter:** Amy Becher-Smith, DNP, MSW, PMHNP, FNP
- **Faculty Planners:** James Edgar Skye and Barbara Jones Warren, PhD, RN, APRN, PMHCNS-BC, FNAP, FAAN

The following individuals have disclosed that they and/or their spouse/partner has had a financial relationship in the past 12 months:

Faculty Presenter: Roger S. McIntyre, MD, FRCPC

- Consultant: Allergan, Janssen, Lundbeck, Minerva, Neurocrine, Otsuka, Pfizer, Purdue, Shire, Sunovion, and Takeda
- Speakers Bureau: Allergan, Janssen, Lundbeck, Minerva, Neurocrine, Otsuka, Pfizer, Purdue, Shire, Sunovion, and Takeda
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Faculty Presenter: Joseph F. Goldberg MD, MS

- Royalties: American Psychiatric Publishing and Cambridge University Press
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Pretest and Posttest Questions

QUESTION 1

A patient presents at your office with a depressive episode and no comorbidities. Of the list below, what would be considered a clue that this patient might have bipolar depression and not unipolar depression?

A. The patient began experiencing depression at age 26

B. The patient has experienced multiple prior episodes (≥5)

C. The patient's current episode has lasted for >6 months

D. The patient has experienced initial insomnia/reduced sleep

E. The patient has a tendency to blame others

B is the correct answer. A patient with bipolar depression is more likely to have "multiple prior episodes (≥5)" than a patient with unipolar depression. Other clinical clues for bipolar depression include an early onset of depression (<25 years), a positive family history of bipolar disorder, hypersomnia/increased daytime napping, hyperphagia/increased weight, atypical depression signs, psychomotor retardation, psychotic features/pathological guilt, mood lability/irritability/psychomotor agitation/racing thoughts, postpartum affective symptoms, substance abuse, and anxiety disorders. On the other hand, clinical clues for unipolar depression include, late onset of first depression (>25 years), long duration of current episode (>6 months), negative family history of bipolar depression, initial insomnia/reduced sleep, appetite/weight loss, normal or increased activity levels, somatic complaints, a tendency to blame others, and anxiety.

Reference: McIntyre RS, Calabrese JR. Bipolar depression: the clinical characteristics and unmet needs of a complex disorder. *Curr Med Res Opin*. 2019;35(11):1993-2005.

Pretest and Posttest Questions (cont.)

QUESTION 2

A 57-year-old man with a 20+ year history of bipolar I disorder, generalized anxiety disorder, and obesity has been maintained on divalproex 1250 mg/day (serum [valproate]=74 mcg/mL) and risperidone 1 mg/day. He now presents with a 1-month period of depressed mood, anhedonia, poor sleep, passive suicidal thoughts, poor concentration, and low self-worth. He also describes feeling inner tension and fast thoughts and speaks with rapid, clipped speech. Which one of the following would be the most evidence-based intervention for this patient?

A. Switch risperidone to lurasidone

B. Augment with lamotrigine

C. Add paroxetine 10 mg/day

D. Add bupropion XL 150 mg/day

E. Switch risperidone to ziprasidone

A is the correct answer. Lurasidone, unlike any of the other choices, has demonstrated efficacy as compared to placebo in randomized controlled trials in bipolar depression. Additionally, lurasidone has shown efficacy to treat bipolar depression with mixed features, as illustrated in the present case.

Reference: McIntyre RS, Cucchiaro J, Pikalov A, Kroger H, Loebel A. Lurasidone in the treatment of bipolar depression with mixed (subsyndromal hypomanic) features: post hoc analysis of a randomized placebo-controlled trial. *J Clin Psychiatry*. 2015;76(4):398-405.

Pretest and Posttest Questions (cont.)

QUESTION 3

A 35-year-old patient with bipolar I disorder elects to go with treatment with an atypical long-acting injectable (LAI) antipsychotic. Which of the following is true of the current FDA-approved LAI antipsychotics for bipolar I disorder?

A. LAIs have a lower risk of extrapyramidal symptoms (EPS) than the oral formulations

B. LAIs have demonstrated efficacy in preventing depression

C. LAIs have demonstrated efficacy in preventing mania

D. LAIs have been shown to prevent comorbidity

E. LAIs are only for schizophrenia

C is the correct answer. When tested as a maintenance monotherapy, both FDA-approved LAI antipsychotics (twice-monthly risperidone and once-monthly aripiprazole) have demonstrated efficacy in delaying the time to recurrence of any mood episode. When examined by type of mood episode, these LAIs have demonstrated efficacy in preventing mania but not depression. Please note, in the aripiprazole LAI trial, patients were currently experiencing a manic episode at study entry, while patients in the risperidone LAI trial either had a recent or current manic or mixed episode. No studies are available in index depression.

One should note that the 2018 Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) guidelines do cite level 4 evidence (uncontrolled trial, anecdotal reports, or expert opinion) for risperidone LAI as an adjunctive agent for the prevention of depression.

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Pretest and Posttest Questions (cont.)

QUESTION 4

Mary is a 22-year old female college student. She was recently diagnosed with bipolar I disorder after being hospitalized for her first episode of mania. She is currently living with her mother, who provides support. She reports sleeping 4 hours per night and has been using marijuana over the past week. Which of the following facts about Mary put her at increased risk for medication nonadherence?

A. Mary is female

B. Mary is a college student

C. This was Mary's first mood episode

D. Mary lives with her mother

E. Mary is using marijuana

The correct answer is E. The Canadian Network for Mood and Anxiety Treatment and International Society for Bipolar Disorder Guidelines (2018) outline the risk factors for partial adherence or nonadherence to medication. Sociodemographic factors include **male**, younger age, **low level of education**, and single. Comorbid factors include alcohol or **cannabis use**. Chronology factors include younger age of onset, current inpatient status, and hospitalization or suicide attempt in the past 12 months. Disease characteristics include mixed episode, rapid cycling, delusions and hallucinations, greater severity of illness, bipolar I disorder diagnosis, and **higher number of episodes**.

Mary's use of marijuana, younger age, hospitalization in the past 12 months, and bipolar I disorder diagnosis put Mary at increased risk for medication nonadherence.

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