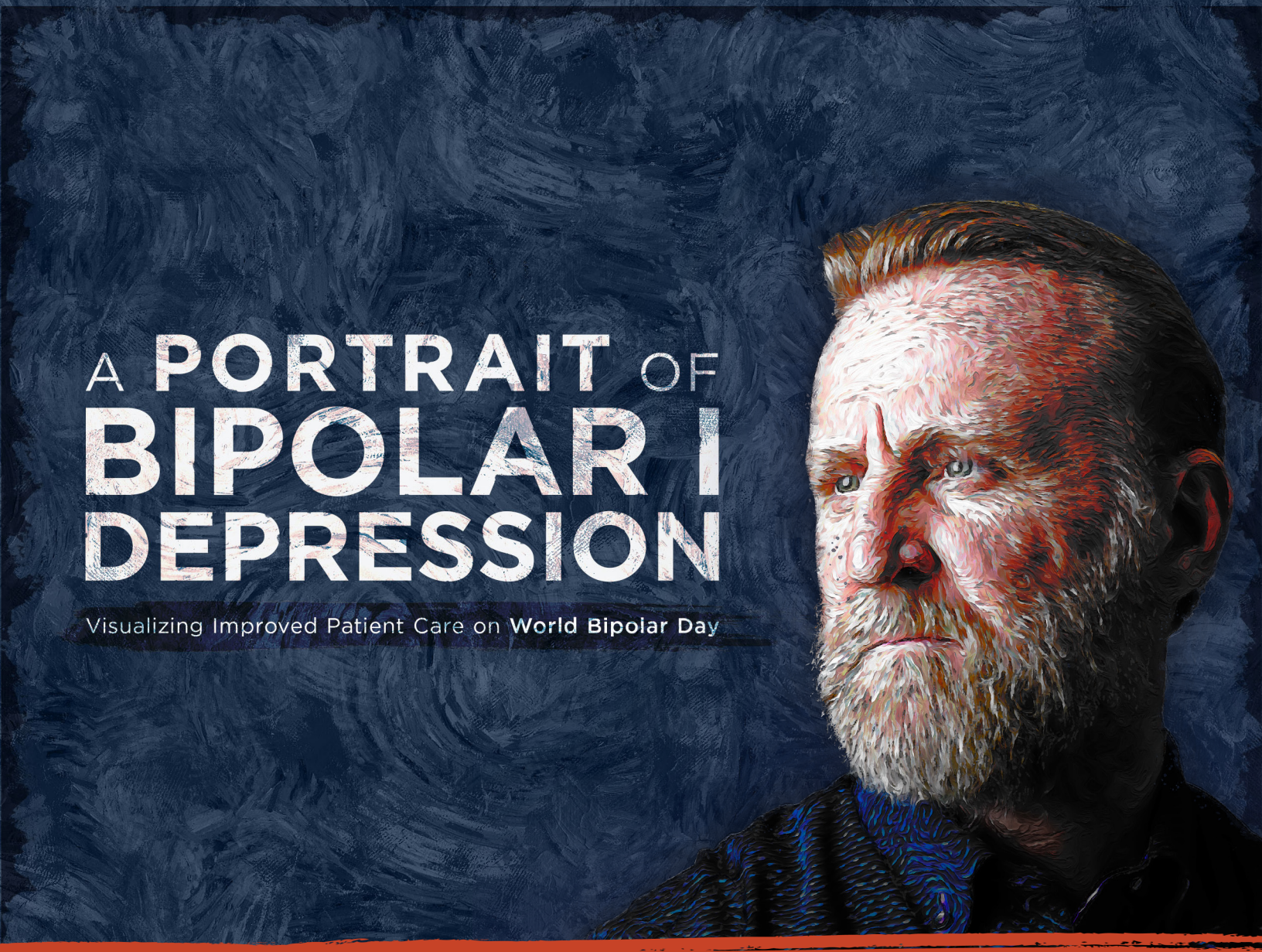

ADDITIONAL RESOURCES

Provided by

forefront COLLABORATIVE

AKH Inc. Advancing Knowledge in Healthcare

This activity is supported by an educational grant from Allergan.
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ACTIVITY DESCRIPTION

Bipolar depression remains a burden for patients living with bipolar I disorder. Therefore, faculty experts came together on World Bipolar Day in a call to action to the healthcare community to improve the diagnosis and treatment of bipolar I depression. In this 60-minute activity previously aired as a live broadcast, faculty review the diagnosis and treatment of a patient case, discussing the utility of tools in diagnosis and strategies to overcome common clinical challenges. An overview of treatments recommended for bipolar I depression will also be provided.

ACTIVITY AGENDA

Welcome
Dr. Goldberg

TED Talks–Style Presentation: A Call to Action—The Need for Earlier, More Accurate Diagnosis and Improved Treatment of Bipolar I Depression
Dr. Goldberg

Patient Case: Diagnosing Sam
Dr. Culpepper, Dr. Goldberg, and Dr. Nierenberg

Question and Answer Session
Dr. Culpepper, Dr. Goldberg, and Dr. Nierenberg

Presentation: Overview of Treatments Recommended for Bipolar I Depression
Dr. Nierenberg

Patient Case (cont.): Treating Sam
Dr. Culpepper, Dr. Goldberg, and Dr. Nierenberg

Question and Answer Session
Dr. Culpepper, Dr. Goldberg, and Dr. Nierenberg

Closing Remarks
Dr. Goldberg

Note: This activity is a recording of a previously aired broadcast. The patient cases not presented in the video are available for download as an additional resource on the activity page.

LEARNING OBJECTIVES

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

1. Distinguish bipolar I depression from unipolar depression earlier in patients.
2. Incorporate tools to help diagnose bipolar I depression into routine practice.
3. Explain the current evidence supporting or opposing use of treatments for bipolar I depression.
4. Develop evidence-based management plans for bipolar I depression.

FACULTY PRESENTER BIOGRAPHIES

Larry Culpepper, MD, MPH

Professor of Family Medicine,
Boston University School of Medicine
Boston, Massachusetts

Larry Culpepper, MD, MPH, is Professor of Family Medicine and was Founding Chairman of the Department of Family Medicine at the Boston University School of Medicine in Massachusetts. He received his medical degree from Baylor College of Medicine in Houston, Texas, and his MPH from Boston University. Dr. Culpepper has conducted federally funded studies of depression and anxiety, otitis media, and school- and community-based interventions to improve pregnancy outcomes and to prevent teen pregnancies. He is a member of the Depression and Bipolar Support Alliance, the Anxiety and Depression Association of America, and the National Sleep Foundation Scientific Advisory Boards and is the editor of the Primary Care Companion for CNS Disorders. Dr. Culpepper served as President of the North American Primary Care Research Group (NAPCRG) and was Co-Principle Investigator of the Primary Care Anxiety Project. He is a recipient of the NAPCRG Society of Teachers of Family Medicine (STFM) Career Research Award, the STFM Excellence in Education Award, and the NAPCRG Maurice Wood Lifetime Research Award, and in 1998 he was elected to the National Academy of Medicine.

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, New York. Dr. Goldberg attended college at The University of Chicago, received his Master of Science in Neuroscience at the University of Illinois-Chicago, and completed medical school at Northwestern University in Chicago. He then 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, he was site principal investigator for the National Institute of Mental Health (NIMH) Systematic Treatment Enhancement Program for Bipolar Disorder program. Dr. Goldberg's research has focused on the clinical psychopharmacology of bipolar and other mood and psychotic disorders. He has received funding from the NIMH, the National Alliance for Research on Schizophrenia & Depression, the American Foundation for Suicide Prevention, and the Stanley Medical Research Institute. 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 2021. 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 by Castle Connolly as one of America's Top Doctors.

FACULTY PRESENTER BIOGRAPHIES (CONT.)

Andrew A. Nierenberg, MD

Thomas P Hackett, MD Endowed Chair in Psychiatry,
Director, Dauten Family Center for Bipolar Treatment Innovation
Co-Director, MGH Center for Clinical Research Education
Massachusetts General Hospital
Professor of Psychiatry, Harvard Medical School
Boston, Massachusetts

Andrew A. Nierenberg, MD, is Thomas P Hackett, MD Endowed Chair in Psychiatry, Director of the Dauten Family Center for Bipolar Treatment Innovation, and Co-Director of the Center for Clinical Research Education at Massachusetts General Hospital and Professor of Psychiatry at Harvard Medical School in Boston, Massachusetts. He received his medical degree from the Albert Einstein College of Medicine in Bronx, New York. After completing a residency in Psychiatry at New York University/Bellevue Hospital in New York, New York, he studied Clinical Epidemiology at Yale University in New Haven, Connecticut, as a Robert Wood Johnson Clinical Scholar. Dr. Nierenberg then joined the faculty at Harvard Medical School, first at McLean Hospital in Belmont, Massachusetts, and then at Massachusetts General Hospital. He is also Honorary Professor at Deakin University's Faculty of Health in Geelong Australia, and Honorary Skou Professor at Aarhus University in Denmark.

Dr. Nierenberg has published more than 525 papers and has been listed in The Best Doctors in America for the treatment of mood and anxiety disorders in every edition since 1994. In 2000, he was awarded the Gerald L. Klerman Young Investigator Award and in 2014 the Gerald L. Klerman Senior Investigator Award by the Depression Bipolar Support Alliance. In 2013, Dr. Nierenberg was awarded the prestigious Brain and Behavior Research Foundation Colvin Prize for outstanding achievement in mood disorders research. In 2014, he was awarded the Mentorship Award for Exceptional Mentorship in the Research Arena at Massachusetts General Hospital. In 2014, 2015, 2016, and 2017, he was listed among the World's Most Influential Scientific Minds by Clarivate in recognition of ranking among the top 1% of researchers for most cited papers in psychiatry worldwide, currently with more than 30,000 citations and an h-factor >85. In 2020, Dr. Nierenberg was given the International Society for Bipolar Disorder Mogen Schou Research Award, the highest award given by the organization.

Dr. Nierenberg was on the leadership teams of the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) and the Sequential Treatment Alternatives to Relieve Depression (STAR*D) National Institute of Mental Health contracts, clinical trials that included thousands of patients with mood disorders. He then led the Bipolar Trials Network to conduct comparative effectiveness studies (LiTMUS and Bipolar CHOICE). He is currently the principal investigator for the Patient Centered Outcomes Research Institute Mood Patient Powered Network plus three Patient-Centered Outcomes Research Institute studies.

FACULTY PLANNER BIOGRAPHIES

Mary D. Moller, DNP, PhD(h), ARNP, PMHCNS-BC, CPRP, FAAN
Associate Professor,
Coordinator, Psychiatric Mental Health-DNP Program
Pacific Lutheran University School of Nursing
Director of Psychiatric Services,
Northwest Integrated Health
Tacoma, Washington

Mary D. Moller, PhD(h), DNP, ARNP, PMHCNS-BC, CPRP, FAAN, is Associate Professor and Coordinator of the Psychiatric Mental Health-DNP Program at the Pacific Lutheran University School of Nursing in Tacoma, Washington and Director of Psychiatric Services at Northwest Integrated Health in Tacoma, Washington. She is an Advanced Registered Nurse Practitioner dually certified as a clinical specialist in adult psychiatric mental health nursing and a psychiatric rehabilitation practitioner. Dr. Moller received her master's degree in Psychiatric Mental Health nursing from the University of Nebraska Medical Center College of Nursing in Omaha and her Doctor of Nursing Practice degree from Case Western Reserve University in Cleveland, Ohio. She received the Case Western Dean's Legacy Award for her research titled The Lived Experience of the Patient with Schizophrenia in the Postpsychotic Adjustment Phase of Recovery from Psychosis. Dr. Moller has authored more than 80 articles, book chapters, conference proceedings, training manuals, policy statements, and is co-author of a best-selling undergraduate psychiatric nursing textbook published by Pearson entitled Psychiatric-Mental Health Nursing: From Suffering to Hope, 2nd edition that received a 2020 American Journal of Nursing Book of the Year Award. She has delivered more than 1000 professional and research presentations both nationally and internationally. She has lectured/consulted in all 50 states, Australia, British Columbia, China, Cuba, Denmark, England, Hong Kong, Israel, Ontario, Saskatchewan, Singapore, and Spain. She has received numerous awards, including the Psychiatric Nurse of the Year from the American Psychiatric Nurses Association, NAMI Professional of the Year, APNA Distinguished Service Award, APNA Award for Clinical Excellence, AAPPN Award for Clinical Excellence, Distinguished Alumnus from the University of Nebraska College of Nursing, and induction as a Fellow in the American Academy of Nursing. She served as President of the American Psychiatric Nurses Association in 2010.

FACULTY PLANNER BIOGRAPHIES (CONT.)

James Edgar Skye
The Bipolar Writer

James Edgar Skye is a native of Salinas, California. He was diagnosed with bipolar I disorder in 2007, and his journey with this disease heavily influences his writing. Mr. Skye's experience with bipolar I helped create the moniker and his brand "The Bipolar Writer." He considers himself an adult and fiction fantasy fiction novelist, but he also writes screenplays and is a memoirist with his company The Bipolar Writer Ghostwriting Services.

In his spare time, when he is not writing fiction, Mr. Skye writes small blog articles that chronicle his issues relating to his mental illness, such as anxiety, depression, insomnia, panic disorder, and suicide. He wrote a memoir on his experiences titled *The Bipolar Writer: A Memoir* released in March 2020. He is also writing/editing a fantasy fiction novel titled *The Rise of Nephilim*, which will be a six-book series. In 2020, Mr. Skye published a short novella and two short stories. The novella is called "Angel on the Ward" and the short stories are titled "The Dark Passenger" and "Hyeon and the Precious Notebook."

Mr. Skye graduated from Southern New Hampshire University with a Bachelor of Fine Arts degree in English and Creative Writing with a specialization in fiction (minoring in journalism and political science). In 2018, he started down the path of completing his Master of Fine Arts Degree in English and Creative Writing with a focus in fiction.

TARGET AUDIENCE

This activity is designed for psychiatrists, primary care physicians (PCPs), nurse practitioners (NPs), and physician assistants (PAs) who care for patients with bipolar I disorder.

ACCREDITATION AND CREDIT DESIGNATION STATEMENTS

Physicians

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

ACCME: Forefront Collaborative designates this 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.

ABIM MOC: Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 1.0 Medical Knowledge MOC points in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

ABPN MOC: The American Board of Psychiatry and Neurology has reviewed A Portrait of Bipolar I Depression: Visualizing Improved Patient Care on World Bipolar Day and has approved this program as part of a comprehensive continuing medical education (CME) program, which is mandated by the ABMS as a necessary component of continuing certification.

Nurse Practitioners

AANP | American Association of NURSE PRACTITIONERS®

This activity has been planned and implemented in accordance with the Accreditation Standards of the American Association of Nurse Practitioners (AANP) through the joint providership of AKH Inc., Advancing Knowledge in Healthcare and Forefront Collaborative. AKH Inc., Advancing Knowledge in Healthcare is accredited by the American Association of Nurse Practitioners as an approved provider of nurse practitioner continuing education. Provider number: 030803.

This activity is approved for 1.0 contact hour (which includes 0.25 hour(s) of pharmacology).

DISCLOSURE OF CONFLICT OF INTEREST

Educational activities provided by Forefront Collaborative and AKH must demonstrate balance, independence, and scientific rigor. All those in a position to control the content of an activity must disclose all relevant financial relationship(s) with commercial interest(s)*. For this educational activity, all conflicts of interest have been resolved through peer review and revisions to ensure independence, evidence base, fair balance, and absence of commercial bias. Disclosures appear below.

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/CE activity:

- Planners (Forefront Collaborative): Valerie Siclari, PhD, and Megan Ragan
- Planners and Reviewers (AKH Inc): Dorothy Caputo, MA, BSN, RN, and Bernadette Marie Makar, MSN, APRN, BC, NP-C
- Faculty Planner: James Edgar Skye

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

Faculty Presenter: Larry Culpepper, MD, MPH

- Royalty: UpToDate
- Consulting Fee: AbbVie Pharmaceuticals, Acadia Pharmaceuticals, Allergan Pharmaceuticals, Eisai Pharmaceuticals, Takeda Pharmaceuticals
- Advisory Board: AbbVie Pharmaceuticals, Acadia Pharmaceuticals, Allergan Pharmaceuticals, Eisai Pharmaceuticals, Takeda Pharmaceuticals
- Ownership Interest: M3 Information, LLC
- Other: Receive payment from Physicians Postgraduate Press as Editor in Chief of the Primary Care Companion for CNS Diseases

Faculty Presenter: Joseph F. Goldberg, MD, MS

- Royalty: American Psychiatric Publishing; Cambridge University Press
- Consulting Fee: BioXcel; Otsuka; Neurocrine; Sunovion; Sage Pharmaceuticals
- Speakers Bureau: AbbVie; Intracellular Therapies; Sunovion
- Advisory Board: Otsuka; Sunovion; Neurocrine

Faculty Presenter: Andrew A. Nierenberg, MD

- Royalty: UpToDate; Guilford Press
- Consulting Fee: Alkermes; Clexio; Ginger.io; Merck; Neuronetics; NeuroRx; Sage; Sunovion
- Contracted Research: Fitbit; Myriad

Faculty Planner: Mary D. Moller, DNP, PhD(h), ARNP, PMHCNS-BC, CPRP, FAAN

- Speakers Bureau: Alkermes; Otsuka
- Advisory Board: Teva

All of the relevant financial relationships listed for these individuals have been mitigated.

*The ACCME defines a commercial interest as any entity producing, marketing, reselling, or distributing health care goods or services consumed by or used on patients. The ACCME does not consider providers of clinical service directly to patients to be commercial interests – unless the provider of clinical service is owned, or controlled by, an ACCME-defined commercial interest.

PRE- AND POSTTEST QUESTIONS

QUESTION 1

Mary is a 24 year old who has had two prior episodes of depression (2 and 5 years ago) during which she responded well to a serotonin–norepinephrine reuptake inhibitor (SNRI). She returns noting that she is feeling depressed following a traumatic romantic breakup and is having difficulty with performance at work. Her Patient Health Questionnaire-9 (PHQ-9) score is 16, and she denies having suicidal thoughts. You carefully evaluated her for bipolar depression when she presented with her first episode and found no indication of a previous (hypo)manic interval.

What should you do next?

A. Given her previous depressive episodes, it is reasonable to immediately restart her SNRI and evaluate for other diagnoses, including bipolar disorder, if she does not respond.

B. Given the recurring episodes, augmenting her SNRI with an atypical antipsychotic is indicated.

C. Evaluate her for post-traumatic stress disorder (PTSD) given the traumatic breakup and treat with medication that will improve it as well as her depression.

D. Evaluate for bipolar depression (eg, using a validated questionnaire) even though you ruled out bipolar disorder in a prior episode.

E. Refer her for an interpersonal therapy given that the combination of her relationship problems in her personal and professional life may be underlying her depressive symptoms.

The correct answer is D.

25-40% of patients diagnosed with bipolar disease have had prior episodes of major depression, and this is more likely in those with depressive episodes in early adulthood or their teenage years. Screening for intercurrent (hypo)manic episodes as part of the initial assessment of every depressive episode is required to make the timely diagnosis of conversion from unipolar to bipolar disease and identify potential for iatrogenic complications of inappropriate or ineffective treatment.

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PRE- AND POSTTEST QUESTIONS (CONT.)

QUESTION 2

Jake was a 28-year-old college dropout with persistent depression living with his parents. He reports depressed mood throughout the day most days, trouble concentrating, no motivation, sleeping 14 hours a day, and passive suicidal thoughts. He spends days smoking weed and playing video games and drinks a six-pack or two of beer "a few nights per week." He did not improve after trials of paroxetine 40 mg/day, escitalopram 20 mg/day, sertraline 150 mg/day, bupropion 300 mg/day, aripiprazole 5 mg/day and quetiapine 50 mg/day. His mother feels that Jake is "self-medicating" and can have sudden anger outbursts, punching walls when upset. Because her maternal grandfather was "diagnosed as manic depressive," she worries that Jake may have "bipolar tendencies" and should be taking other medications. His PHQ-9 score is 26, Mood Disorder Questionnaire (MDQ) score is 4 and hypomania checklist (HCL-32) score is 8.

Which of the following would be an appropriate next step in Jake's management?

A. Rediagnose Jake as having bipolar I depression based on his family history, nonresponse to multiple antidepressants, "staying up much of the night," and "anger outbursts" that could be construed as depressive episodes with mixed features.

B. Rule out a probable diagnosis of bipolar disorder based on Jake's PHQ-9 score.

C. Tell Jake and his mother that his substance use could interfere with his response to medications and could be worsening his mood. To clarify his diagnosis and treatment, Jake needs to gain some period of abstinence and have his mood reassessed.

D. Diagnose Jake as having bipolar II disorder because that designation accounts for ambiguity about the presence of distinct "high" periods.

The correct answer is C.

Jake's cannabis and alcohol use disorder pose significant confounding factors either for making a comorbid psychiatric diagnosis or judging the apparent low efficacy of past pharmacotherapy trials. While it is true that many individuals with bipolar disorder have comorbid substance use disorders, the psychoactive effects of current substance use can masquerade as primary mood symptoms or otherwise alter the presentation of an underlying mood or other psychiatric disorder.

Jake's PHQ-9 screen indicates a high level of depressive symptom severity (it does not provide information about current or lifetime mania symptoms), but how much of his current depression may be influenced by substance-induced mood changes is difficult to estimate. His MDQ score of 4 falls below the established cut-off threshold for identifying likely casehood for bipolar disorder in psychiatric settings (≥7). In depressed primary care patients, an MDQ threshold score of ≥5 has been described with high sensitivity (0.91) and moderate specificity (0.67), while an HCL-32 of ≥15 yielded a sensitivity of 0.64 and specificity of 0.57. Notably, in mood disordered patients with active substance use disorders, the MDQ has shown low positive predictive value (0.38), but high negative predictive value (0.86), meaning that a subthreshold score indicates a very low likelihood for casehood.

In the setting of active substance use, the application of the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) criteria would lead to a provisional diagnosis of psychoactive substance-induced mood disorder. A period of sustained abstinence (likely, at a minimum, 1 month) would allow for the reassessment of Jake's mood with less potential contamination from the effects of cannabis and alcohol.

Of further note, Jake's report of persistent rather than episodic or phasic periods of depression would be more consistent with unipolar than bipolar disorder. Although we are told that he "stays up all night" we are also told that he sleeps for 14 hours at a time, well into the next day, indicating more of a delayed sleep-wake phase circadian dysrhythmia than a "manic" decreased need for sleep. His reported anger outbursts can be multi-determinate; anger outbursts have been reported in major depressive disorder, substance use disorders, and personality disorders, among other conditions, and do not by themselves indicate bipolar disorder. Family history can be a useful corroborative feature of bipolar disorder, although its penetrance and likely clinical impact is substantially less in a second- rather than first-degree relative.

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PRE- AND POSTTEST QUESTIONS (CONT.)

QUESTION 3

Which of the following statements are TRUE about antidepressant monotherapy for bipolar I depression?

A. Antidepressant monotherapy has proven efficacy for the treatment of bipolar I depression.
B. Antidepressant monotherapy has a low probability of being effective for bipolar I depression.
C. Antidepressant monotherapy has shown an increased risk for suicidal thoughts or behaviors in patients with bipolar I depression.
D. Antidepressant monotherapy has not been shown to trigger manic episodes and rapid cycling in patients with bipolar I depression.

The correct answer is B.

Meta-analyses reveal that the greatest risk when using antidepressants for individuals with bipolar disorder is the very low likelihood of response. A review by Sidor and Macqueen identified a disappointingly high number-needed-to-treat (NNT) for response of 29. The largest prospective randomized trial of monoaminergic antidepressants in bipolar depression (STEP-BD) found no higher rates of response among mood stabilizer recipients who took an antidepressant (bupropion or paroxetine) versus a mood stabilizer plus placebo. Studies of antidepressant use in bipolar depressed patients have not shown an increased risk for suicidal thoughts or behaviors as compared to patients not taking antidepressants (eg, STEP-BD), and in fact some naturalistic studies report significant reductions in suicidality (by as much as 20%) among patients with bipolar disorder prescribed antidepressants over multiyear follow-ups (eg, the 27-year Collaborative Depression Study). Antidepressant monotherapy use in bipolar depression has been found to trigger manic episodes and rapid cycling. In one study, 55% of patients with bipolar disorder previously diagnosed with depression became manic, and 23% became rapid cyclers on antidepressants. In another study, 73% of rapid cyclers were taking antidepressants when their cycling began. Rapid cycling is associated with poorer treatment response and a worse prognosis.

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PRE- AND POSTTEST QUESTIONS (CONT.)

QUESTION 4

Michelle was a 53-year-old obese, hypertensive woman who has been treated for depression and anxiety with benzodiazepines, desipramine 100 mg at night, and perphenazine. She has "ups and downs" and has never felt a sustained even mood. Her husband says Michelle was briefly hospitalized at age 22 after the birth of their daughter when she could not sleep for days, stopped eating and talking, and felt that she had to die to save her daughter's soul. She responded to electroconvulsive therapy (ECT) with subsequent placement on desipramine. Her husband says Michelle can "go for weeks or months of lying in bed during the day" followed by "bursts of energy" with nonstop talking, excessive social plans, and maxing out credit cards. Currently, she reports moderate depression and anxiety, fitful sleep, low motivation, "comfort eating" and sees no point in living but would never act on suicidal thought. Her PHQ-9 score is 19.

All of the following would be appropriate next steps in Michelle's treatment EXCEPT:

A. Measure her desipramine level and ensure it is in the therapeutic range; if subtherapeutic, increase the dose and continue to monitor.
B. Discontinue the desipramine and replace with lithium plus lamotrigine.
C. Discontinue the desipramine and replace with cariprazine.
D. Discontinue the desipramine and replace with lurasidone.

The correct answer is A.

The history is consistent with bipolar I disorder based on (apparently unrecognized) periods of high energy, psychomotor acceleration and impulsive risk-taking that jeopardizes functioning ("maxing out credit cards"), interspersed with periods of depression. The history also suggests illness onset that began with a postpartum psychotic depression, with postpartum onset and psychotic depression both representing risk factors for the eventual development of bipolar disorder. Michelle's symptoms have apparently persisted with an undulating course despite long-term treatment with desipramine, suggesting lack of efficacy as well as a possible destabilizing effect. While tricyclic antidepressants such as desipramine are sometimes considered an appropriate pharmacotherapy for relapse prevention after ECT, they are considered a particularly risky proposition for induction of mania or cycle acceleration in people with bipolar disorder. The 2018 CANMAT/ISBD guidelines do not recommend antidepressant monotherapy for bipolar I depression due to a lack of demonstrated efficacy for bipolar I depression and safety concerns (level 2 negative).

Michelle now presents with symptoms consistent with a major depressive episode. Lithium (level 2 evidence) and adjunctive lamotrigine (level 2 evidence) are recommended as first-line treatments for acute bipolar depression in the 2018 CANMAT/ISBD guidelines. Lithium plus lamotrigine is an evidence-based but off-label pharmacotherapy option for bipolar depression. Lurasidone (level 2 evidence) is recommended as a first-line treatment and cariprazine (level 2 evidence) is recommended as a second-line treatment for acute bipolar depression in the 2018 CANMAT/ISBD guidelines. Lurasidone and cariprazine are both FDA-approved treatment options for bipolar I depression. Other FDA-approved options include quetiapine and olanzapine-fluoxetine combination, however, Michelle's morbid obesity and overall cardiovascular risk in the setting of hypertension would make both of the latter options less attractive due to their relatively higher metabolic liability.

PRE- AND POSTTEST QUESTIONS (CONT.)

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