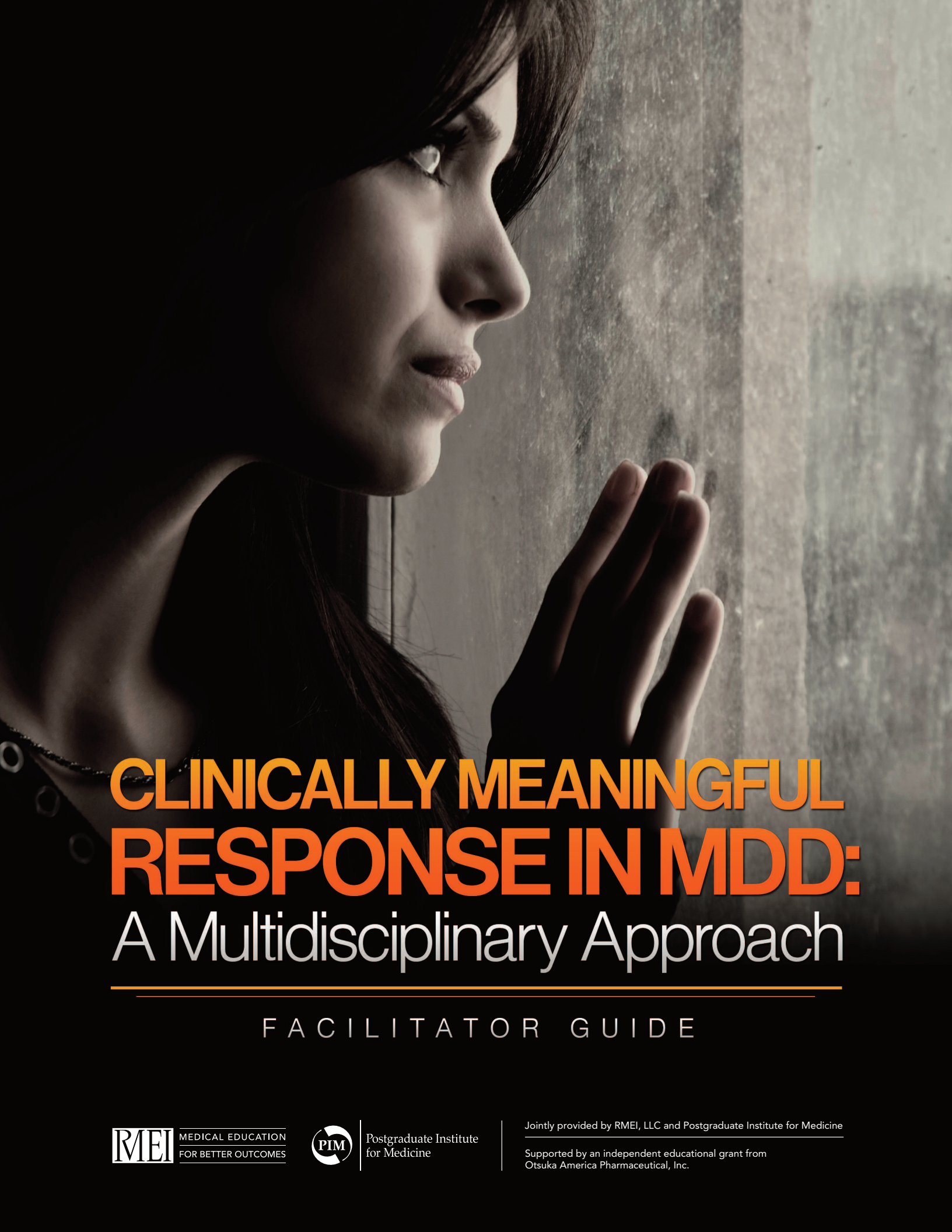

CLINICALLY MEANINGFUL RESPONSE IN MDD: A Multidisciplinary Approach

FACILITATOR GUIDE

RMEI MEDICAL EDUCATION FOR BETTER OUTCOMES

PIM Postgraduate Institute for Medicine

Jointly provided by RMEI, LLC and Postgraduate Institute for Medicine

Supported by an independent educational grant from Otsuka America Pharmaceutical, Inc.

CONTENTS

WELCOME

Dear Mental Health Professional:

Welcome, and thank you for requesting this valuable electronic resource on major depressive disorder (MDD). Despite numerous treatment options for depression, this disorder continues to be inadequately treated, and lack of treatment response and relapse is common. In order to help address the burden posed by substantial morbidity, mortality and healthcare costs (Kessler, Berglund et al. 2003; Stewart, Ricci et al. 2003; Kessler, Chiu et al. 2005; Wang, Lane et al. 2005; Shim, Baltrus et al. 2011) associated with MDD, we have developed this virtual "Program-in-a-Box" resource for mental healthcare providers in the community mental health setting who are involved in the care of patients with MDD.

Unlike other continuing education activities where someone else schedules the activity, this program gives you the flexibility of scheduling the activity when it is convenient for you and your team. Please refer to the next page in this guide for complete instructions on how to use this unique resource.

Educational resources include:

- Program manager who will answer questions and provide assistance via telephone regarding logistics of scheduling and facilitating the program
- Comprehensive program checklist with step-by-step instructions on how to implement the activity. This includes a discussion topic prompt to encourage participants to utilize the educational activity as an opportunity to huddle and discuss gaps and barriers to appropriate management of treatment non-response in your facility. In addition, the discussion of mechanisms for overcoming gaps based on the content provided.
- Customizable flyer so the activity can be promoted to your internal staff
- Workbook that you can download and print (if applicable) prior to the meeting (workbook includes slides, references, speaker biographies, and CE information)
- URL for the online slide-audio program
- Sign-in sheet
- Instructions for submitting questions electronically for the MDD experts
- Post-test/continuing education (CE) evaluation form
- Transmittal sheet
- Options for returning completed post-test/CE evaluations, sign-in sheet and program checklist

On behalf of the joint providers for this activity, RMEI, LLC and Postgraduate Institute for Medicine, I would like to thank you for your interest. We hope that you find the information provided to be useful in improving the quality of care for patients with MDD. If you have any questions about this activity, please contact Marie Laney at (856) 672-3354. To learn more about other free educational activities offered by RMEI, LLC, visit us at http://www.rmei.com/.

Sincerely,

Jacqui Brooks, MBBCh, MRCPsych
Senior Vice President, Medical Strategy
RMEI, LLC

INSTRUCTIONS

Instructions for using Program-in-a-Box:
In order to ensure the most effective use of this Program-in-a-Box, you should follow these important instructions:

Organize and promote your educational activity:

1. Organize a meeting of your colleagues at your institution.
2. To promote your meeting, please customize the electronic version of the flyer provided to you and make copies for distribution and/or posting.
   - Fill in the date and time of your meeting on the flyer, and post it in your institution. Please allow 1 hour for the completion of this activity.
     - Participants should spend 45 minutes viewing the presentation
     - Participants should spend 15 minutes discussing the material and completing the post-test/CE evaluation form
3. Distribute the workbook to attendees by making copies or send the PDF electronically in advance. The workbooks contain pertinent continuing education information and copies of slides that are in the presentation.

Conduct your educational activity:

1. You will need the following equipment in order to conduct your activity:
   - A computer with internet access and internal or external speakers
   - An LCD projector and screen
2. Assemble your audience consisting of psychiatrists, registered nurses, nurse practitioners, physician assistants, psychologists, social workers, and case managers.
3. Open your internet browser and go to the URL provided.
   - Click on the “Start Lecture” button at the bottom of the screen as shown:

4. Provide instructions for generating and submitting questions for the MDD experts.
   - You can send any questions to MDDeducation@RMEI.com and RMEI will provide them to the faculty and will email a response to the submitter as soon as possible after the program.

Continues on the Following Page ➔

INSTRUCTIONS

Conclude your educational activity:

1. At the conclusion of the program, ask each participant to complete the post-test/CE evaluation forms provided for download.
2. Collect all post-test/CE evaluation forms, sign-in sheets and program checklist and return with the completed transmittal sheet in one of the following ways:
   a. Scan all materials and e-mail to: MDDeducation@RMEI.com
   b. Complete the post-test/CE evaluation at CME University. PIM supports Green CME by offering your Request for Credit online. If you wish to receive acknowledgment for completing this activity, please complete the post-test and evaluation on www.cmeuniversity.com. On the navigation menu, click on "Find Post-test/Evaluation by Course" and search by course ID 10193. Upon registering and successfully completing the post-test with a score of 70% or better and the activity evaluation, your certificate will be made available immediately. Processing credit requests online will reduce the amount of paper used by nearly 100,000 sheets per year.
   c. Mail paper copies to: RMEI, LLC
      Attn: Marie Laney
      Laurel Office Plaza
      101 Laurel Road, Suite 200
      Voorhees, NJ 08043
   d. Request a self-addressed, stamped envelope to return your materials by contacting Marie Laney at (856) 672-3354
3. Certificates of continuing education credit will be provided to participants who complete the post-test/CE evaluation and score at least 70%. Certificates will be emailed within 4-6 weeks upon receipt of completed post-test/CE evaluation forms. If facilitators submit scanned or mailed post-tests/CE evaluations, Postgraduate Institute for Medicine will email participant a certificate which is proof of passing. Those participants that did not pass the post-test/CE evaluation will be provided instructions to log on to CME University to try again. If the post-test/CE evaluation is completed on CME University, the system will grade post-tests automatically and participants will immediately see results.
   - This activity is eligible for continuing education credit from October 28, 2014, through October 28, 2015.

OVERVIEW

TARGET AUDIENCE

This activity has been designed to meet the educational needs of psychiatrists, registered nurses, nurse practitioners, physician assistants, psychologists, social workers, and case managers who manage patients with major depressive disorder (MDD).

STATEMENT OF NEED

Major depressive disorder (MDD) affects 7.1% of individuals each year and 14.4% of individuals over the course of a lifetime (Kessler, Petukhova et al. 2012) and is associated with substantial morbidity, mortality and healthcare costs (Kessler, Berglund et al. 2003; Stewart, Ricci et al. 2003; Kessler, Chiu et al. 2005; Wang, Lane et al. 2005; Shim, Baltrus et al. 2011).

Despite numerous treatment options for depression, this disorder continues to be inadequately treated, and lack of treatment response and relapse is common. The Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study examined responses of a large cohort of MDD patients who underwent up to four successive treatment steps. This study demonstrated that only about 30–40% of patients with MDD attain full remission with first- or second-line treatment (Rush, Trivedi et al. 2006; Trivedi, Rush et al. 2006; Sinyor, Schaffer et al. 2010; Perlis 2013). Even after instituting third- and fourth-line treatments, which included a multitude of switching and augmentation strategies, only 67% achieved remission. The results of this study underscored the limitations of current options to treat to meaningful clinical improvement as well as the fact that responses to current antidepressant options are suboptimal.

Current strategies for managing treatment non-response and resistance in MDD include dose optimization, switching antidepressant medications or medication classes, and augmenting therapy by adding another treatment, such as a different medication or psychotherapy (Thase 2011). Focusing on neurotransmitters other than serotonin may advance treatment for resistant MDD; this can be achieved by utilizing combination therapy with lithium, atypical antipsychotics and other pharmacological agents (Mathews, Henter et al. 2012; Schlaepfer, Agren et al. 2012; Murrough, Iosifescu et al. 2013; Pehrson and Sanchez 2013). Other options include transcranial magnetic stimulation (TMS), which has been shown to have a modest effect in patients with treatment-resistant depression, and electroconvulsive therapy, which is usually reserved for severe treatment-resistant MDD or MDD with psychotic or catatonic features (APA 2010; Lee, Hermens et al. 2012). Deep brain stimulation (DBS) is another option, generally reserved as a last resort (Schlaepfer, Agren et al. 2012).

MDD management often falls short of achieving meaningful clinical response because not all symptoms of depression are uniformly well-recognized (Ravnkilde, Bruun et al. 2007; Rizzo 2008). Clinical diagnosis of MDD remains challenging for caregivers, as both patients and physicians have difficulty accurately evaluating the symptoms (Mitchell, Vaze et al. 2009; Tyrer 2009). Clinicians and patients may also fail to recognize that multiple MDD symptoms can contribute to poor response (Mitchell, Vaze et al. 2009; Tyrer 2009).

Due to the frequency of inadequate response to MDD treatment, additional therapeutic options are greatly needed. New MDD drug development efforts have focused on therapeutics with reduced side effects in order to improve patient adherence to treatment plans (Sheehan, Croft et al. 2009; Baldwin, Hansen et al. 2012). A larger variety of neurotransmitter targets are also being explored beyond the serotonergic and noradrenergic systems that may result in improved response rates and assist in addressing some of the symptoms of MDD that are overlooked by currently available therapies.

APA. Practice Guideline for Treatment of Patients With Major Depressive Disorder. Washington, D.C., *American Psychiatric Association Press*. 2010.

Baldwin DS, Hansen T, et al. Vortioxetine (Lu AA21004) in the long-term open-label treatment of major depressive disorder. *Curr Med Res Opin*. 2012;28(10):1717–1724.

Kessler RC, Berglund P, et al. (2003). The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). *JAMA*. 2003;289(23):3095–3105.

Kessler RC, Chiu WT, et al. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005;62(6):617–627.

Kessler RC, Petukhova M, et al. Twelve-month and lifetime prevalence and lifetime morbid risk of anxiety and mood disorders in the United States. *Int J Methods Psychiatr Res*. 2012;21(3):169–184.

Lee RS, Hermens DF, et al. A meta-analysis of cognitive deficits in first-episode Major Depressive Disorder. *J Affect Disord*. 2012;140(2):113–124.

Mathews DC, Henter ID, et al. Targeting the glutamatergic system to treat major depressive disorder: rationale and progress to date. *Drugs*. 2012;72(10): 1313–1333.

Mitchell AJ, Vaze A, et al. Clinical diagnosis of depression in primary care: a meta-analysis. *Lancet*. 2009; 374(9690):609–619.

Murrough JW, Iosifescu DV, et al. Antidepressant efficacy of ketamine in treatment-resistant major depression: a two-site randomized controlled trial. *Am J Psychiatry*. 2013 Oct 1;170(10):1134–1142. doi: 10.1176/appi.ajp.2013.13030392.

Pehrson AL, Sanchez C. Serotonergic modulation of glutamate neurotransmission as a strategy for treating depression and cognitive dysfunction. *CNS Spectr*. 2013;1–13.

Perlis RH. A clinical risk stratification tool for predicting treatment resistance in major depressive disorder. *Biol Psychiatry*. 2013;74(1):7–14.

Ravnkilde B, Bruun LM, et al. Cognitive symptoms of depression—importance for treatment and prognosis. *Ugeskr Laeger*. 2007;169(16):1459–1462.

Rizzo ALR. Major depression and explicit memory. *Iatreia*. 2008;21(2):177–185.

Rush AJ, Trivedi MH, et al. Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: a STAR*D report. *Am J Psychiatry*. 2006;163(11):1905–1917.

Schlaepfer TE, Agren H, et al. The hidden third: improving outcome in treatment-resistant depression. *J Psychopharmacol*. 2012;26(5):58–-602.

Sheehan DV, Croft HA, et al. Extended-release trazodone in major depressive disorder: a randomized, double-blind, placebo-controlled study. *Psychiatry (Edgmont)*. 2009;6(5):20–33.

Shim RS, Baltrus P, et al. Prevalence, treatment, and control of depressive symptoms in the United States: results from the National Health and Nutrition Examination Survey (NHANES), 2005–2008. *J Am Board Fam Med*.2011;24(1):33–38.

Sinyor M, Schaffer A, et al. The sequenced treatment alternatives to relieve depression (STAR*D) trial: a review. *Can J Psychiatry*. 2010;55(3):126–135.

Stewart WF, Ricci JA, et al. Cost of lost productive work time among US workers with depression. *JAMA*. 2003;289(23):3135–3144.

Thase ME, Trivedi MH, et al. MAOIs in the contemporary treatment of depression. *Neuropsychopharmacology*. 1995;12(3):185–219.

Trivedi MH, Rush AJ, et al. Factors associated with health-related quality of life among outpatients with major depressive disorder: a STAR*D report. *J Clin Psychiatry*. 2006;67(2):185–195.

Tyrer P. Are general practitioners really unable to diagnose depression? *Lancet*. 2009;374(9690):589–590.

Wang PS, Lane M, et al. Twelve-month use of mental health services in the United States: results from the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005;62(6):629–640.

EDUCATIONAL LEARNING OBJECTIVES

After participating in this educational initiative, participants will be able to:

- Utilize comprehensive history-taking and assessment tools to monitor for, and identify, inadequate treatment response and residual symptoms in major depressive disorder (MDD)
- Implement appropriate treatments for MDD that address all symptoms of the disorder, including new and emerging antidepressants
- Integrate into practice strategies for managing patients with partial response or non-response in MDD
- Provide appropriate care and counsel for patients and their families

STATEMENT OF SUPPORT

This program is jointly provided by RMEI, LLC and Postgraduate Institute for Medicine, and is supported by an independent educational grant from Otsuka America Pharmaceutical, Inc.

TENTATIVE MEETING AGENDA

5 minutes ..... *Welcome, Introductions, Program-In-A-Box Description*

10 minutes..... *PowerPoint Presentation: Assessing Response to Treatment in MDD*
Includes discussion of utilizing history and assessment/screening tools in assessing treatment response in MDD

10 minutes..... *Patient Case Challenge and Faculty Discussion*
Assessing Treatment Response in MDD

15 minutes..... *PowerPoint Presentation: Improving Response to Antidepressant Therapy*
Includes discussion of management approaches to improve treatment response in MDD, including new and emerging treatment options

10 minutes..... *Patient Case Challenge and Faculty Discussion*
Approaches to Improving Treatment Response in MDD

10 minutes..... Q&A, Group Discussion, and Post-Test/Evaluation

FACULTY BIOGRAPHIES

Michael E. Thase, MD

Professor of Psychiatry
Perelman School of Medicine at the University of Pennsylvania
Philadelphia Veterans Affairs Medical Center
Philadelphia, Pennsylvania

Michael E. Thase, MD, joined the faculty of the University of Pennsylvania School of Medicine in January, 2007, as Professor of Psychiatry and director of the Department of Psychiatry's Mood and Anxiety Section after more than 27 years at the University of Pittsburgh Medical Center and the Western Psychiatric Institute and Clinic. Dr. Thase also directs the Mood Disorders Research studies at the Philadelphia VAMC.

A 1979 graduate of the Ohio State University College of Medicine, Dr. Thase is a Distinguished Fellow of the American Psychiatric Association, a Founding Fellow of the Academy of Cognitive Therapy, a member of the Board of Directors of the American Society of Clinical Psychopharmacology, and Vice Chairman of the Scientific Advisory Board of the National Depression and Bipolar Support Alliance. Dr. Thase has been elected to the membership of the American College of Psychiatrists and the American College of Neuropsychopharmacology.

Dr. Thase's research, which has been continuously funded by the Institutes of the NIH for nearly 30 years, focuses on the assessment and treatment of mood disorders, including studies of the differential therapeutics of both depression and bipolar affective disorder. Current research projects include studies of novel ketamine-like compounds, a multicenter study of the efficacy of rTMS for depressed veterans (funded as a cooperative study by the VHA), a multicenter trial comparing the effectiveness and tolerability of lithium and quetiapine for bipolar depression (funded by AHRQ and conducted as part of the Bipolar Treatment Network), and a large-scale noninferiority trial comparing a novel computer-administered form of cognitive therapy versus the conventional 20 session/16 week model of treatment (two-center trial funded by NIMH, with J. Wright of University of Louisville). Dr. Thase has authored or co-authored more than 600 scientific articles and book chapters, as well as 16 books.

FACULTY BIOGRAPHIES

Denise Vanacore, PhD, CRNP, ANP-BC, PMHNP

Associate Professor of Nursing
Director Doctor of Nursing Practice and Nurse Practitioner Programs
Gwynedd Mercy University
Gwynedd Valley, Pennsylvania

Dr. Denise A. Vanacore is the Director of Primary Care and Psychiatric Services as well as an Adult and Psychiatric Nurse Practitioner at the Health Center in Lansdale, Pennsylvania. In addition she is the Director of the Doctor of Nursing Practice and Nurse Practitioner Programs, and Associate Professor of Nursing at Gwynedd-Mercy University in Gwynedd Valley, Pennsylvania. She received her PhD in nursing from Walden University and her Master's degree in nursing as an adult nurse practitioner, as well as her Bachelor's and Master's degrees in nursing, from Gwynedd Mercy University. Dr. Vanacore received a post-master's certification as a Psychiatric Mental Health Nurse Practitioner from Drexel University in Philadelphia. She received a second Master's degree in nursing with a focus on academic education from Villanova University, Villanova, Pennsylvania, and completed her postgraduate fellowship in psychiatric services at the University of Pennsylvania Hospital, Philadelphia. Dr. Vanacore is an RN in Pennsylvania, New Jersey, and Delaware and has her NP license in Pennsylvania and New Jersey. She has expertise in psychiatric-mental health, the primary and psychiatric care of individuals, care of patients with intellectual disabilities and the management and administration of primary care and psychiatric practice. In addition, she has worked extensively in the areas of general and psychiatric assessment and pharmacology.

Dr. Vanacore has presented nationally and internationally and has authored several articles, several chapters in textbooks, and an assessment textbook manual. She is also the recipient of the Gwynedd-Mercy University Alumni Award for Professional Achievement and the Sigma Theta Tau Region 6 Research Award in clinical practice. She is a member of the American Nurses Association, American Psychiatric Nurses Association, National League for Nursing, American Academy of Nurse Practitioners, National Organization of Nurse Practitioner Faculty, Sigma Theta Tau, the Iota Kappa Chapter (international honor society for nursing), among many others. Dr. Vanacore is the Chair of the AANP national taskforce on depression and anxiety in primary care.

ACCREDITATION & CREDIT

CONTINUING EDUCATION INFORMATION

PHYSICIAN CONTINUING EDUCATION

Accreditation Statement

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of Postgraduate Institute for Medicine and RMEI, LLC. The Postgraduate Institute for Medicine is accredited by the ACCME to provide continuing medical education for physicians.

Credit Designation

The Postgraduate Institute for Medicine designates this live activity for a maximum of 1.25 *AMA PRA Category 1 Credit*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

NURSING CONTINUING EDUCATION

Credit Designation

This educational activity for 1.2 contact hours is provided by Postgraduate Institute for Medicine.

Accreditation Statement

Postgraduate Institute for Medicine is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

SOCIAL WORKER EDUCATION

Postgraduate Institute for Medicine, Provider Number 5114
Course meets the qualifications for 1.25 hours of continuing education credit for MFTs, LPCCs, LEPs and/or LCSWs as required by the California Board of Behavioral Sciences.

FEE INFORMATION

There is no fee for this educational activity.

DISCLOSURES

DISCLOSURE OF CONFLICTS OF INTEREST

Postgraduate Institute for Medicine (PIM) requires instructors, planners, managers and other individuals who are in a position to control the content of this activity to disclose any real or apparent conflict of interest (COI) they may have as related to the content of this activity. All identified COI are thoroughly vetted and resolved according to PIM policy. PIM is committed to providing its learners with high quality CME activities and related materials that promote improvements or quality in healthcare and not a specific proprietary business interest of a commercial interest.

The ***faculty*** reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:

- **Michael E. Thase, MD**, has affiliations with Alkermes, AstraZeneca, Bristol-Myers Squibb Company, Cerecor, Inc., Eli Lilly & Co., Dey Pharma, L.P., Forest Laboratories, Gerson Lehman Group, GlaxoSmithKline, Guidepoint Global, H. Lundbeck A/S, MedAvante Inc., Merck and Co. Inc., Neuronetics, Inc., Novartis, Otsuka, Ortho-McNeil Pharmaceuticals, Pamlab, L.L.C., Pfizer, Shire US Inc., Sunovion Pharmaceuticals, Inc., Supernus Pharmaceuticals, Takeda, Transcept Pharmaceuticals *(Consultant)*; Agency for Healthcare Research and Quality, Alkermes, Eli Lilly and Company, Forest Pharmaceuticals, National Institute of Mental Health, Otsuka Pharmaceuticals, PharmaNeuroboost, Roche *(Grant Support)*; MedAvante, Inc. *(Equity Holdings)*; American Psychiatric Foundation, Fuilford Publications, Herald House, W.W. Norton & Company, In., *(Royalties)*, Peloton Advantage *(Other: spouse employed)*.
- **Denise Vanacore, PhD, CRNP, ANP-BC, PMHNP**, has no affiliations with commercial interests to disclose.

The ***planners*** and ***managers*** reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:

RMEI, LLC

- **Jacqui Brooks, MBBCh, MRCPsych**, has no affiliations with commercial interests to disclose.
- **Nora Hartley, MLIS,** has no affiliations with commercial interests to disclose.
- **Lillian McVey** has no affiliations with commercial interests to disclose.
- **Elise M. Paxson** has no affiliations with commercial interests to disclose.

Postgraduate Institute for Medicine

The following PIM planners and managers, **Laura Excell, ND, NP, MS, MA, LPC, NCC, Trace Hutchison, PharmD, Samantha Mattiucci, PharmD, CCMEP, and Jan Schultz, RN, MSN, CCMEP**, hereby state that they or their spouse/life partner do not have any financial relationships or relationships to products or devices with any commercial interest related to the content of this activity of any amount during the past 12 months.

DISCLOSURE OF UNLABELED USE

This educational activity may contain discussion of published and/or investigational uses of agents that are not indicated by the FDA. The planners of this activity do not recommend the use of any agent outside of the labeled indications.

The opinions expressed in the educational activity are those of the faculty and do not necessarily represent the views of the planners. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications, and warnings.

DISCLAIMER

DISCLAIMER

Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not meant to serve as a guideline for patient management. Any procedures, medications, or other courses of diagnosis or treatment discussed or suggested in this activity should not be used by clinicians without evaluation of their patient's conditions and possible contraindications and/or dangers in use, review of any applicable manufacturer's product information, and comparison with recommendations of other authorities.

NOTES