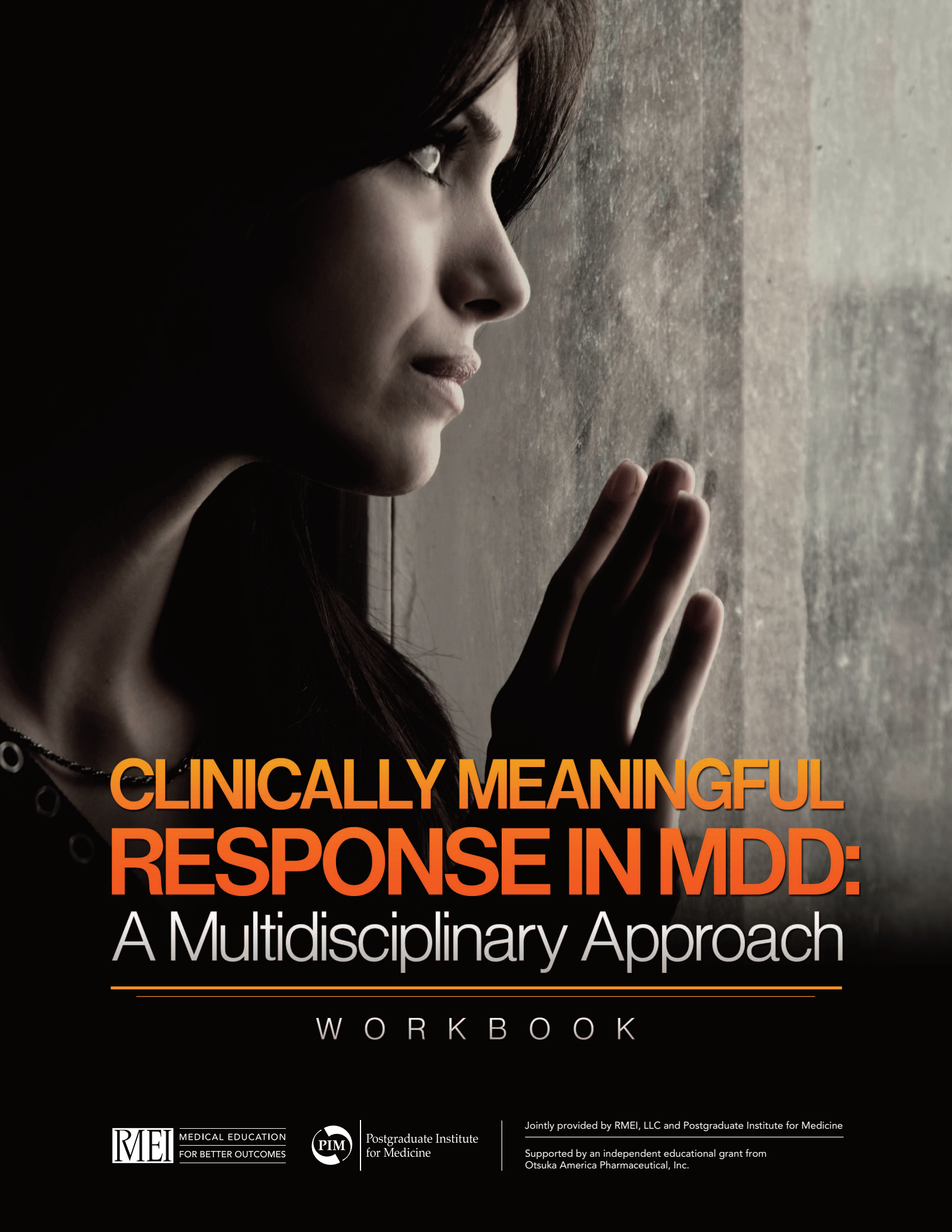

CLINICALLY MEANINGFUL RESPONSE IN MDD:

A Multidisciplinary Approach

WORKBOOK

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

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.

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

MEETING AGENDA

Overview . . . . . 5 minutes
Presentation . . . . . 45 minutes
Q&A Session . . . . . 10 minutes

FACULTY BIOGRAPHY

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 BIOGRAPHY

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.

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- **Denise Vanacore, PhD, CRNP, ANP-BC, PMHNP**, has no affiliations with commercial interests to disclose.

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- **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.

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.

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Assessing Response to Treatment in MDD

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Introduction

- Maintain a high index of suspicion for the presence of treatment-resistant depression
- The relationship between medical conditions and depression is complex
- Depression may exacerbate coexisting medical illness and may make it more difficult to treat
- Some medications may cause, contribute or worsen depression
- Late-life depression may be overlooked if inadequately treated

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Assessment

- Thorough interview and clinical history on each encounter
- Mental status examination
- Screening measures
- Tracking signs and symptoms of current depressive episode including intensity of symptoms

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Some Risk Factors for Treatment-Resistant Depression

- Comorbidities
- Alcohol or substance abuse
- History of attempted suicide
- History of psychiatric hospitalization
- Early age of onset of depression
- Higher body mass index (BMI)
- Personal or family history of depression or mood disorder
- Anxiety disorder

Most Important Comorbid Conditions

- Alcohol dependence
- Cerebrovascular diseases
- Medications that can cause mood disorders
- Neurodegenerative disorders (e.g., Alzheimer disease, Parkinson disease, multiple sclerosis)
- Substance abuse
- Sleep apnea (40%–60% of patients with dementia)

Carroll VK, Rado JT. *Current Psychiatry.* 2009;8:43–54

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Laboratory Tests For Evaluating Depression

Common Tests	Tests To Be Considered
• Chemistry profile (electrolytes, blood urea nitrogen, creatinine, glucose) • Complete blood count • Serum levels of anticonvulsant or tricyclic antidepressant, if taking either type of medication • Thyroid function (T3, T4, TSH)	• Electrocardiogram • Vitamin B12 and folate level • Vitamin D • Magnesium level • Serum calcium level • Serum level of digoxin or theophylline, if taking either medication • Urinalysis

Krieg JC. *J Psychiatr Res.* 1994; 28:337–9.

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Medications That May Cause Symptoms of Depression

- Alpha-methyl dopa
- Anabolic steroids
- Anti-arrhythmic medications
- Anticonvulsant medications
- Anti-dementia
- Barbiturates
- Benzodiazepines (i.e., long acting)
- Carbidopa or levodopa
- Certain beta-adrenergic antagonists (propranolol)
- Clonidine
- Cytokines (specifically IL-2, interferon)
- Digitalis preparations
- Glucocorticoids
- H2 blockers
- Metoclopramide
- Opioids

Rogers D, Pies R. *Psychiatry (Edgmont)*. 2008;5:28–41.
Sidhu K, Balon R. *Current Psychiatry*. 2008;7:61–74.

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Screening Tool Considerations

- Characteristics of the population to be screened
- Psychometric properties of the instrument
- Time required to complete the measure
- Time required to score the measure
- Ease of use
- Cost of obtaining the measure

Limitations of Screening Tools

- Important diagnostic features
- Degree of impairment
- Comorbid medical or psychiatric illnesses
- Most are based on criteria prior to the DSM-IV or based on the DSM-IV
- Clinician time
- Literacy

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Rating Scales

- Adopt a policy of formal screening for patients
- Use at the beginning of treatment
- Only reliable way to obtain an objective measure
- Essential to monitoring the effectiveness of treatment
- Improves the identification of patients presenting with depression

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Screening Tools

- Beck Depression Inventory-II (BID-II)
- Center for Epidemiologic Studies of Depression Scale Revised (CESD-R)
- Hamilton Depression Scale (HAM-D)
- Inventory of Depressive Symptomatology (IDS)
- Montgomery-Asberg Depression Rating Scale (MADRS)
- Zung Self-rating Depression Scale (Zung SDS)

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Screening Tools – Short Options

- Clinically Useful Depression Outcome Scale (CUDOS)
- Quick Inventory of Depressive Symptomatology (QIDS)
- Patient Health Questionnaire-9 (PHQ-9)

Special Populations

- Elderly
  - Geriatric Depression Inventory (GDS- 30 or 15)
  - Cornell Scale for Depression in Dementia (CSDD)
- Children and adolescents
  - Children's Depression Inventory (CDI) – Age 7-17
  - Reynolds Child Depression Scale (RCDS) – Age 8-12
  - Patient Health Questionnaire A (PHQ-A) – Adolescents
  - Kutcher Adolescent Depression Scale (KADS)

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Other Screening Tools

- Multiple Sclerosis Depression Rating Scale
- Edinburgh Postnatal Depression Scale
- Neurologic Disorders Depression Inventory for Epilepsy (NIDDI-E)
- Psychiatric Assessment Schedule for Adults with a Developmental Disability (PAS-ADD)

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The PHQ-9

- Is a validated tool to screen for and diagnose depression
- Has also been validated as a tool for measuring response to treatment
- Scoring for each question ranges from 0–3
  - Not at all = 0
  - Several days = 1
  - More than half the days = 2
  - Nearly every day = 3

Kroenke K, et al. *J Gen Intern Med.* 2001;16:606–13.

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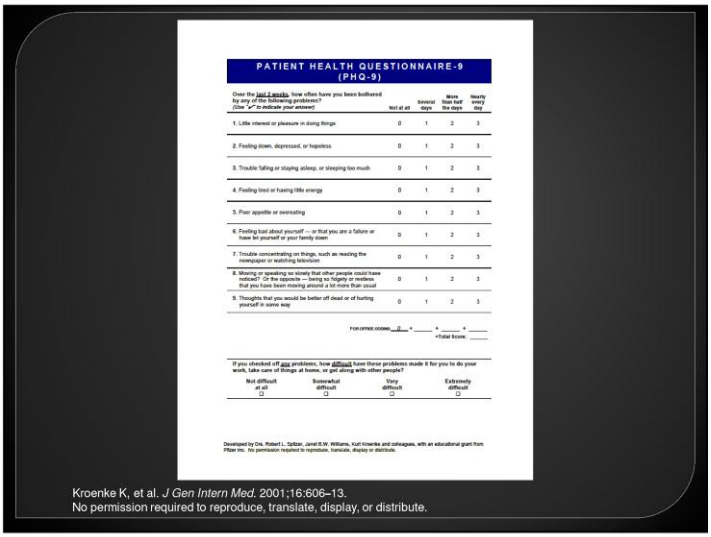
PHQ-9: Interpreting the Total Score

Scores are added together to determine severity of symptoms

Total Score	Depression Severity
1-4	***Minimal Depression***
5-9	***Mild Depression***
10-14	***Moderate Depression***
15-19	***Moderate-Severe Depression***
20-27	***Severe Depression***



Kroenke K, et al. *J Gen Intern Med.* 2001;16:606–13.
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Mood Disorder Questionnaire

- By Hirschfeld RM, Williams JB, Spitzer RL, et al (2000)
- 13-item checklist
- Designed to help determine if a client is likely to have BD
- Screening instrument
- Good sensitivity and specificity
  - Correctly identify 7 of 10 patients with BD
  - 9 of 10 without BD will be correctly screened out

Hirschfeld RM, et al. *Am J Psychiatry.* 2000;157:873–5.

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Monitoring

- Monitor the patient's response to treatment for depression
  - Goals of treatment may include, but need not be limited to, the following:
    - Resolution of signs and symptoms of depression
    - Improvement of scores on the PHQ-9, HAM-D, or CES-D
    - Improvement in attendance at and participation in usual activities
    - Improvement in sleep pattern
- Treatment response can vary widely among depressed patients
- Patient response is generally not predictable before the treatment changes.

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Screening Tool References

- Beck Assessment Tools – Psychological Corporation – http://www.psychcorp.com/
- CESD-R – http://cesd-r.com
- HAM-D – http://healthnet.umassmed.edu/mhealth/HAMD.pdf
- IDS/QIDS – www.ids-qids.org
- MADRS – https://outcometracker.org/library/MADRS.pdf
- Zung – http://healthnet.umassmed.edu/mhealth/ZungSelfRatedDepressionScale.pdf
- CUDOS – www.outcometracker.org
- PHQ – www.phqscreeners.com

Summary

- Accurate diagnosis of depression is important
- To determine impact of treatment especially in treatment resistance, it is necessary to evaluate outcomes by using standardized rating scales
- Depression usually responds to treatment with psychotherapy, medications, or a combination of the two
- Treatment options should be consistent with the patient's and family's wishes

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Patient Case Challenge: Assessing Treatment Response in MDD

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Case Study: Tricia

- 42-year-old woman who presents with daily symptoms of:
  - Sadness, crying
  - Loss of interest in her gardening, cooking, and cleaning
  - Sleeping 9–11 hours per night
  - Feeling very tired
  - Distractibility—unable to read or watch TV
- Initial PHQ-9 = 21

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Guideline for Using the PHQ-9 for Initial Management

Score/ Symptom Level	Treatment
0–4 No depression	▪ Consider other diagnoses
5–9 Minimal	▪ Consider other diagnoses ▪ If diagnosis is depression, watchful waiting is appropriate initial management
10–14 Mild	▪ Consider watchful waiting ▪ If active treatment is needed, medication or psychotherapy is equally effective
15–19 Moderate	▪ Active treatment with medication or psychotherapy is recommended ▪ Medication or psychotherapy is equally effective
20–27 Severe	▪ Medication treatment is recommended ▪ For many people, psychotherapy is useful as an additional treatment ▪ People with severe symptoms often benefit from consultation with a psychiatrist

Case Study: Tricia – Follow-up

- Due to her PHQ-9 she was started on citalopram 10 mg x 1 week and then 20 mg
- At her 4-week visit
  - She had a minimal decrease in symptoms based on frequency
  - Her PHQ-9 score had decreased to: 19
- CBT was added to her treatment plan and the PHQ-9 score was shared with the therapist

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Interpreting Follow-Up Scores

PHQ-9 - Change from last score, measured monthly	Treatment Response	Treatment Plan
Drop of 5 or more points each month	Good	Antidepressant &/or Psychotherapy No treatment change needed. Follow-up in 4 weeks.
Drop of 2-4 points each month	Fair	Antidepressant: May warrant an increase in dose.
		Psychotherapy: Probably no treatment change needed. Share PHQ-9 with psychotherapist.
Drop of 1 point, no change or increase each month	Poor	Antidepressant: Increase dose or augment or switch; informal or formal psychiatric consult; add psychotherapy.
		Psychotherapy: 1. If depression-specific psychotherapy discuss with supervising psychiatrist, consider adding antidepressant. 2. For patients satisfied in non depression specific psychotherapy consider adding antidepressant. 3. For patients dissatisfied in non depression psychotherapy, review treatment options and preferences.

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Case Study: Tricia – Follow-up 2

- Due to her PHQ-9, CBT – twice weekly for 4 weeks
- At her 8-week visit
  - She had a mild decrease in symptoms based on type, frequency, intensity, and duration
  - Her PHQ-9 was 17
- Her citalopram was increased to 40 mg and the CBT was continued twice weekly

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Interpreting Follow-Up Scores

PHQ-9 - Change from last score, measured monthly	Treatment Response	Treatment Plan
Drop of 5 or more points each month	Good	Antidepressant &/or Psychotherapy No treatment change needed. Follow-up in 4 weeks.
Drop of 2-4 points each month	Fair	Antidepressant: May warrant an increase in dose. Psychotherapy: Probably no treatment change needed. Share PHQ-9 with psychotherapist.
Drop of 1 point, no change or increase each month	Poor	Antidepressant: Increase dose or augment or switch; informal or formal psychiatric consult; add psychotherapy. Psychotherapy: 1. If depression-specific psychotherapy, discuss with supervising psychiatrist; consider adding antidepressant. 2. For patients satisfied in other psychotherapy, consider adding antidepressant. 3. For patients dissatisfied in other psychotherapy, review treatment options and preferences.

Conclusions

- Further treatment outcome research comparing scale
- Primary care physicians (PCPs) have embraced responsibility for screening, recognizing, and treating depression
- For additional efficiencies, we will need
  - Advances in technology (e.g., computerized screening and scoring)
  - Improved treatment outcomes

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Improving Response to Antidepressant Therapy

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Antidepressant Drugs: Unmet Needs Circa 2014

- Limited efficacy (~ 10–20% advantage vs PBO in RCTs)
- Intolerable side effects for 10%
- Inconsistent effects on key symptoms (insomnia, anxiety)
- Relatively slow onset of action
- Better alternatives for nonresponders

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Factors to Consider When Selecting an Antidepressant

- Personal & family treatment history
- Track record & ease of use
- Tolerability profile
- Safety profile
- Cost (direct and indirect)

First Line Antidepressants: 2014

- Consensus across guidelines is that the following antidepressants are first-line:
  - Selective serotonin reuptake inhibitors (SSRIs)
  - Serotonin-norepinephrine reuptake inhibitors (SNRIs)
  - Bupropion (norepinephrine-dopamine reuptake inhibitor [NDRI])

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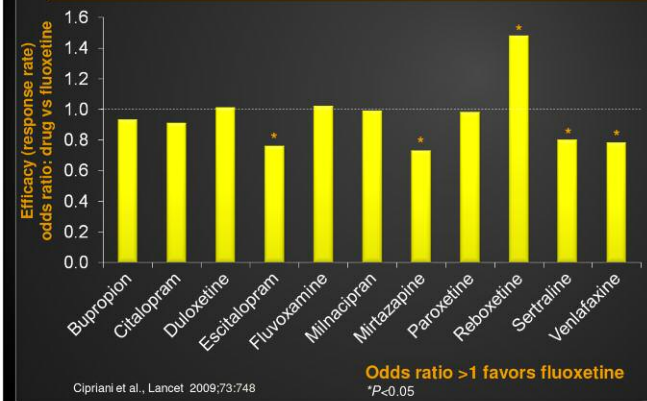
Efficacy (Response Rate) Odds Ratio – Fluoxetine as Reference Compound



Cipriani et al., Lancet 2009;73:748

*$P<0.05$

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Newer Antidepressants

- Vilazodone (2011)
- Lurasidone (2013): BPI depression only
- Levomilnacipran (2013)
- Vortioxetine (2013)

BPI = Bipolar I Depression

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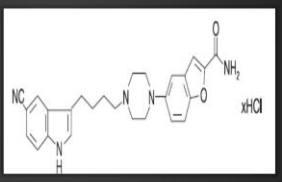
Vilazodone

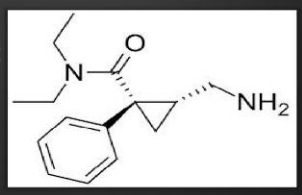
- Approved for MDD in 2011
- MoA: SRI + 5-HT1a partial agonism
- Therapeutic dose: 40 mg/day (requires 3-step titration to minimize nausea)
- Low incidence of sexual side effects
- Still no comparative or switch data



MoA = Mechanism of Action

Levomilnacipran

- Levo enantiomer of milnacipran (sNRI); sustained release formulation
- Better dose-response than racemate?
- Therapeutic dose range: 40–120 mg/day
- Efficacy established in 4 placebo-controlled trials; no comparative data
- Approved by FDA: December 2013



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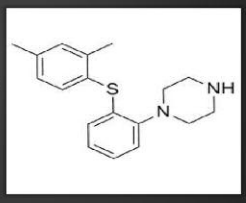
Vortioxetine

- A novel drug classified as a serotonin modulator: SRI & antagonist of 5-HT3 and 5-HT7, complex effects on 5-HT1
- Therapeutic dose range: 5–20 mg/day



- Efficacy established in placebo-controlled trials; generally comparable to duloxetine (5 trials)
- Availability: November (date?)

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What Constitutes an Adequate Trial of an Antidepressant?

- Longer (duration) is generally better (>4 weeks at a full therapeutic dose)
- Whenever possible, the dose should be increased above the minimum
- Intolerance does not equal nonresponse
- Residual symptoms (nonremission) do not equal nonresponse

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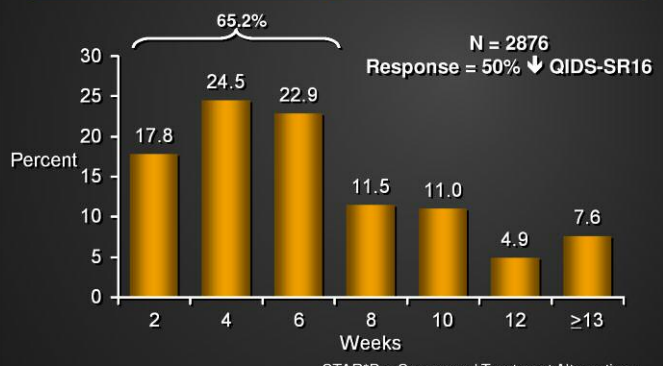
Two-thirds of STAR*D Responders Did So by Week 6



Trivedi et al. *Am J Psychiatry* 2006; 163:28-40

STAR*D = Sequenced Treatment Alternatives to Relieve Depression

Should We Switch or Use Adjunctive Strategies?

- Parsimony favors switching
- Adjunctive therapies often easier to implement
- STAR*D disappointingly did not answer this question

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Common Adjunctive Strategies: 2014

- Lithium and other mood stabilizers
- Thyroid hormones
- Buspirone and BZs
- Methylfolate (Deplin)
- Combining two antidepressants
- 2nd-generation antipsychotics (SGAs)

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Combining Antidepressants: Advanced Practice or Fad?

- Once considered an indicator of bad practice, combining antidepressants is now commonly done for TRD
- Bupropion and mirtazapine now preferred
- No antidepressant has FDA approval for this use and only one (mirtazapine) has the support of two positive studies
- Most newer combos safe; caveats

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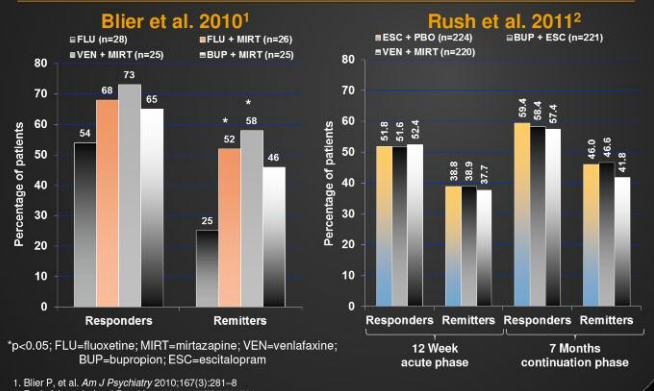
Concurrent Combined Antidepressants: Contrasting Results



*p<0.05; FLU=fluoxetine; MIRT=mirtazapine; VEN=venlafaxine; BUP=bupropion; ESC=escitalopram

1. Blier P, et al. *Am J Psychiatry* 2010;167(3):281–8
2. Rush AJ, et al. *Am J Psychiatry* 2011;168(7):689–701

Are SGAs Antidepressants?

- 4 have established efficacy as adjuncts to antidepressants (aripiprazole, olanzapine, quetiapine, and risperidone)
- 3 have established efficacy as monotherapies in bipolar depression (olanzapine, quetiapine, and lurasidone)
- 1 has established efficacy as a monotherapy in MDD (quetiapine)

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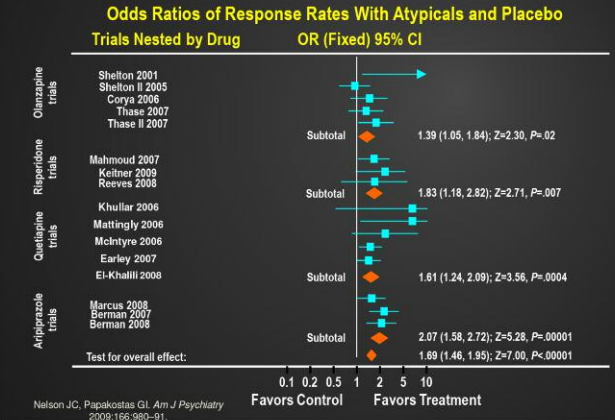
Meta-Analysis of Response Rates in Double-Blind, Placebo-Controlled, Atypical Augmentation Trials



Nelson JC, Papakostas GI. *Am J Psychiatry* 2009;166:980–91.

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Augmentation with SGAs: Important Issues

- Is efficacy sustained?
- Cost effectiveness vs. other options?
- Ultimate risks of tardive dyskinesia and metabolic complications
- Within-class differences:
  - Anxiety?
  - Utility for reverse neurovegetative symptoms?
  - Metabolic risks?

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Neuromodulation Strategies

- Electroconvulsive therapy (ECT)
- Transcranial magnetic stimulation (rTMS)
- Vagus nerve stimulation
- Deep brain stimulation

Conclusions

- Generic SSRIs, SNRIs, and bupropion remain favored 1st-line therapies
- Greatest unmet needs are speed of effect and alternate therapies
- Uncertain to what extent newer antidepressants will fill these needs
- Still unmet need for novel agents

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A Patient With Unremitting Depressive Symptoms

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Patient Presentation

- Mary is a 42-year-old married woman who lives with her husband and 12 year old and works in graphics design
- She was referred by her PCP
- She has a history of a depressive episode that began 6 months ago and has not fully responded despite 12 weeks of escitalopram therapy, including 4 weeks at 20 mg/day

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Mary's Unremitting Symptoms

- Since beginning escitalopram, Mary reports that she has had fewer crying spells and she may be functioning somewhat better at work
- However, she reports marked fatigue and feels like collapsing each evening at home
- She is sleeping about 1–2 hours more than usual and has gained about 3–4 kg despite having little gusto for food
- She reports little joy or drive and describes having to "go through the motions" with her husband and her children

Discussion Points

- Screening for inadequate response to antidepressants:
  - Are we doing a good job?
  - Are we recognizing/diagnosing potential comorbid medical/psychiatric problems?
  - What are the barriers to care in our facility?
- The screening tools we use are helpful: Discuss
- Managing depression that is not adequately responsive to treatment:
  - What are the best approaches to treating depression that does not respond adequately?
  - Do we do a good job?
  - What are the barriers to adequately treating depression to remission?

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