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Recognizing and Responding to Inadequately Treated Major Depressive Disorder (MDD): A Nursing Perspective

Mary D Moller, DNP, ARNP, PMHCNS-BC, CPRP, FAAN
Associate Professor, Pacific Lutheran University School of Nursing, Tacoma WA

Georgia Stevens, PhD, APRN, PMHCNS-BC
Director, P.A.L. Associates
Partners in Aging & Long-term Caregiving
Washington, DC

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Objectives

- Discuss the burden of MDD on the individual and society
- Explore the negative impact of residual symptoms
- Identify patient and treatment characteristics associated with a poor treatment response
- Discuss evidence for the treatment of patients with MDD and practical guidelines

MDD, major depressive disorder.

BURDEN OF MDD

Mary D Moller, DNP, ARNP, PMHCNS-BC, CPRP, FAAN

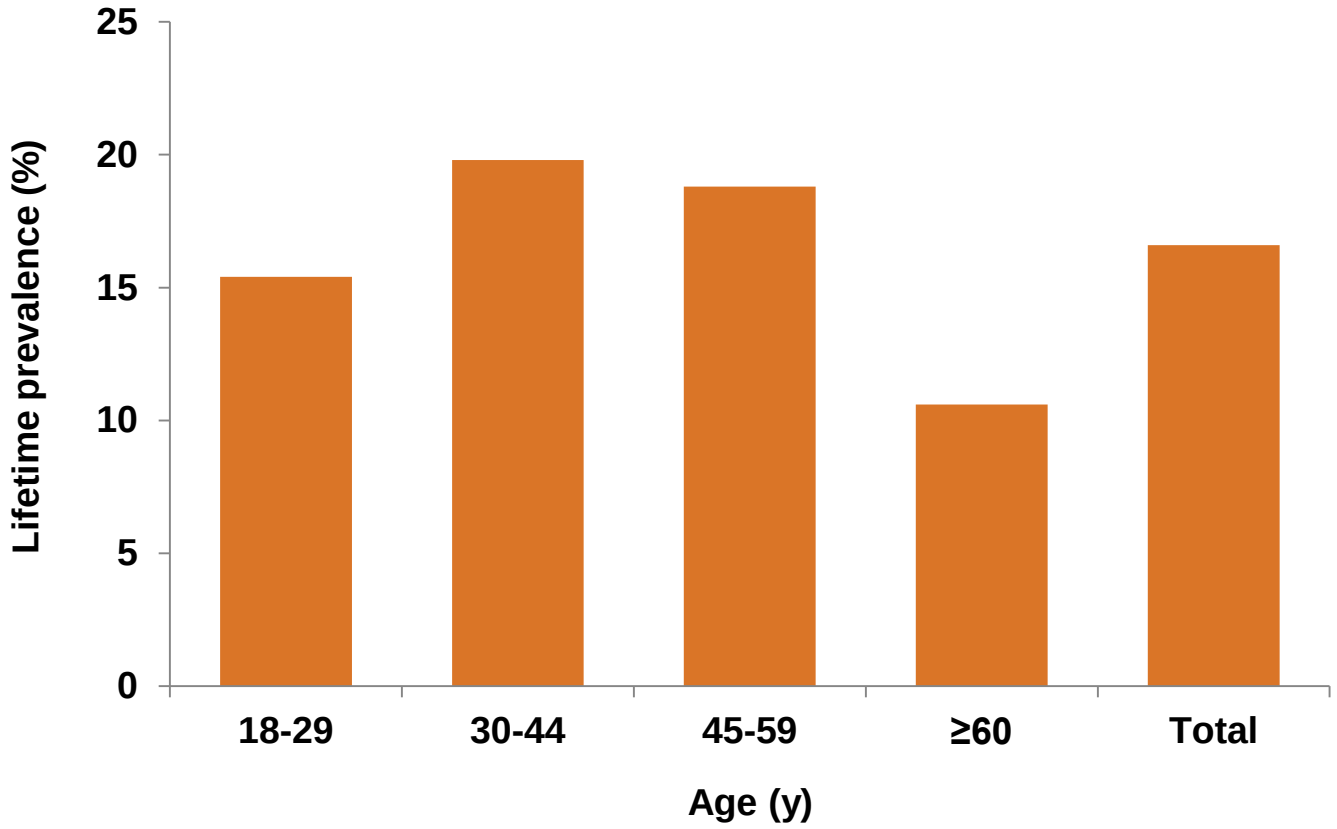
Introduction

- Depression is the most common diagnosis among patients seen by psychiatrists in the US[1]
- MDD is a serious, chronic, disabling illness affecting more than 350 million people worldwide[2]
- MDD results in a substantial burden of disease to both the individual and society[3]
- Residual symptoms are common and cause significant psychosocial and occupational functional impairment[4,5]

MDD, major depressive disorder; US, United States.

1. Duffy FF et al. *Psychiatr Serv.* 2008;59(10):1148-1154;
2. World Health Organization. *Fact Sheet on Depression.* (2012) http://www.who.int/mediacentre/factsheets/fs369/en/index.html;
3. Kessler RC. *Psychiatr Clin North Am.* 2012;35(1):1-14;
4. Romera I et al. *Eur Psychiatry*. 2010;25(1):58-65;
5. Zimmerman M et al. *Compr Psychiatry.* 2007;48(2):113-117.

Lifetime Prevalence of MDD

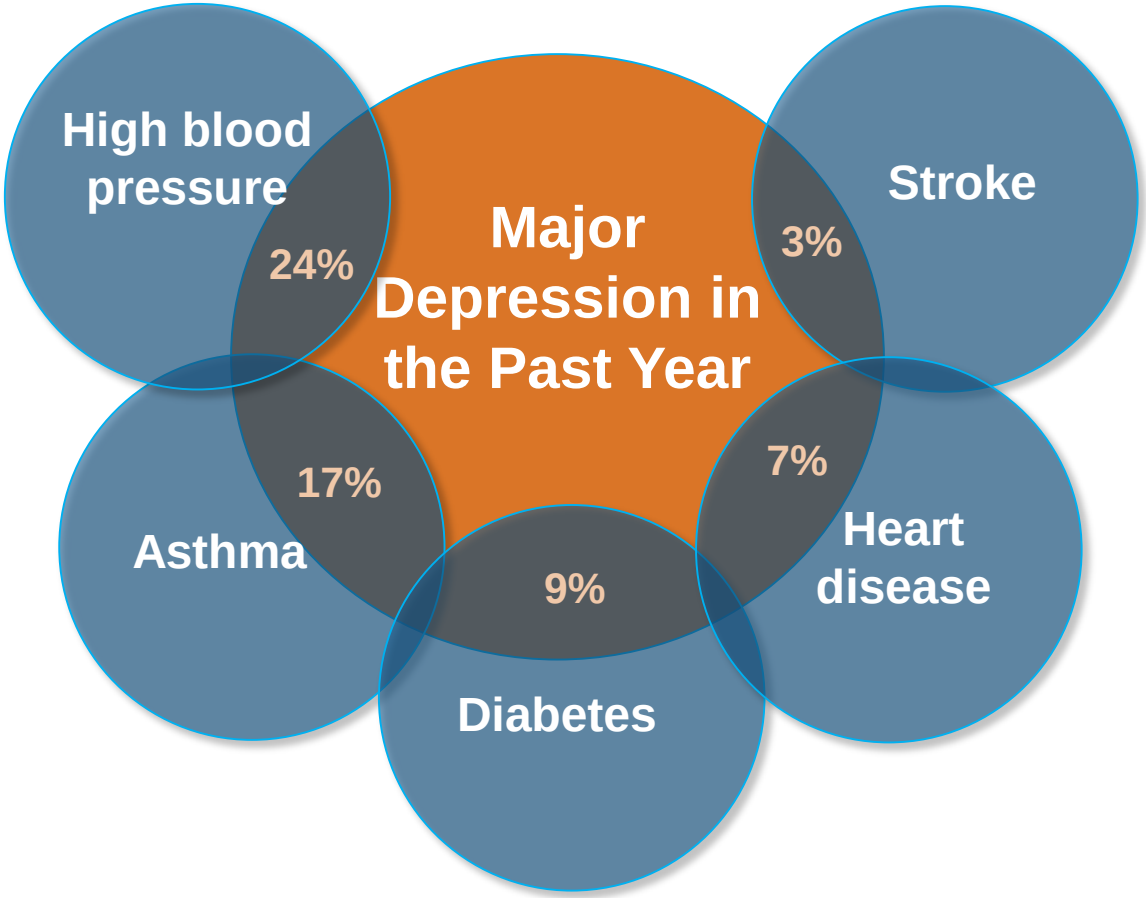


- Overall lifetime prevalence of MDD across all ages is 16.6%

MDD, major depressive disorder.

1. Kessler RC et al. *Arch Gen Psychiatry.* 2005;62(6):593-602

Link Between Depression and Other Illnesses



- When these rates were compared with subjects without reported mental illness in the past year, the differences in all chronic health conditions were statistically significantly different at the 0.05 level

1. www.samhsa.gov/data/2k12/NSUDH103/SR103AdultsAMI2012.htm. Accessed 29 April 2014.

Burden of Disease to the Individual

- Physical:
  - MDD is a consistent predictor of the subsequent first onset of a variety of chronic physical disorders, including arthritis, asthma, cardiovascular disease, diabetes, chronic pain, and certain types of cancer
- Financial:
  - Incomes of people with MDD are substantially lower than those without depression
- Education:
  - MDD is associated with a 60% elevated risk of failure to complete secondary school than otherwise comparable youth

MDD, major depressive disorder.

1. Kessler RC. *Psychiatr Clin North Am*. 2012;35(1):1-14.

Suicide Risk

- Patients with MDD are roughly 20 times more likely to commit suicide than the general population
- Attempts at suicide among patients with MDD are highly associated with the occurrence and overall severity of MDD symptoms
- Increased time spent depressed is predictive of suicide attempts in this population

MDD, major depressive disorder.

1. Sokero TP et al. *Br J Psychiatry*. 2005;186:314-318.

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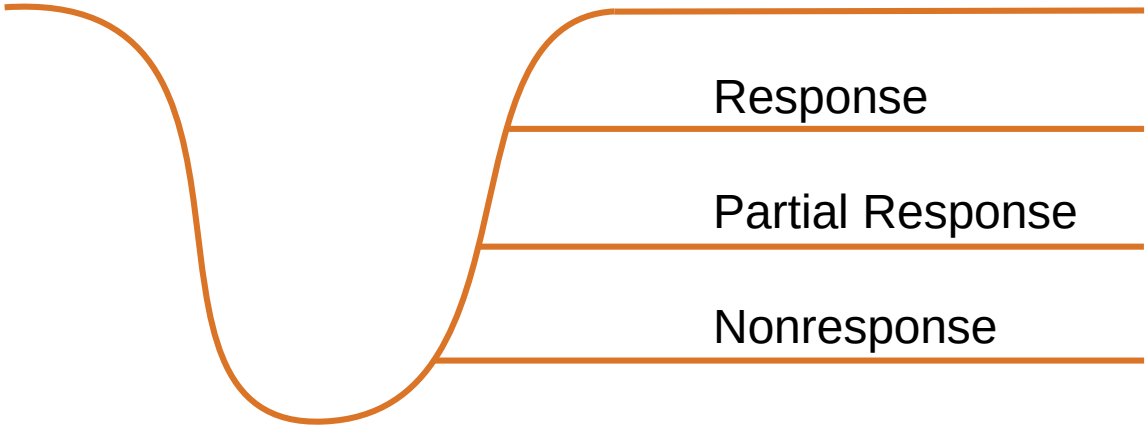
RESIDUAL SYMPTOMS IN MDD

Georgia Stevens, PhD, APRN, PMHCNS-BC

Remission Is the Goal



Remission is also defined as attainment of a virtually asymptomatic status (17-item HAM-D score ≤ 7) for at least 2 consecutive weeks.[3]

HAM-D, Hamilton Depression Rating Scale; MADRS, Montgomery–Åsberg Depression Rating Scale.

1. Weisler R et al. *CNS Spectrums*. 2009;14(6):299-313;
2. Nierenberg AA et al. *J Clin Psychiatry*. 2001;62(suppl 16):5-9;
3. Frank E et al. *Arch Gen Psychiatry*. 1991;48:851-855 et al.

Common Unresolved or Residual MDD Symptoms

Estimated frequencies[1]:

- Sleep disturbances (44%)
- Fatigue (38%)
- Diminished interest or pleasure (27%)
- Guilt (≈ 25%)
- Concentration difficulties (≈ 25%)
- Disturbances in mood (≈ 15%)
- Weight issues (≈ 15%)
- Disturbances in psychomotor activity (≈ 5%)
- Suicidal ideation (≈ 5%)

Other residual/unresolved MDD symptoms include: core mood symptoms,[2] anxiety,[2,3] irritability and/or inner tension,[3] somatic symptoms (including pain),[2,4] sexual dysfunction,[3] and impairment of work and/or activities[2]

MDD, major depressive disorder.

1. Nierenberg AA et al. J Clin Psychiatry. 1999;60(4):221-225.
2. Romera I et al. *BMC Psychiatry*. 2013;13:51;
3. Trivedi MH et al. *J Clin Psychiatry*. 2008;69(2):246-258;
4. Trivedi MH. *J Clin Psychiatry*. 2004:6(Suppl 1)12-16.

Impact of Residual Symptoms on Patient Functioning and Outcomes

- Residual symptoms cause significant and often persistent psychosocial and occupational functional impairment[1,2,3]
- Patients being treated for MDD who have residual symptoms have an increased risk of depressive relapse[4,5]

Author	N	Time Followed	Relapsed
Paykel[4]	70	15 months	▪ 76% of patients with residual symptoms ▪ 25% of patients with no residual symptoms
Pintor[5]	139	4 years	▪ 91% of patients with partial remission ▪ 51% of patients with complete remission

- Patients with residual symptoms tend to have poor psychosocial functioning[6]

MDD, major depressive disorder.

1. Romera I et al. *Eur Psychiatry*. 2010;25(1):58-65;
2. Zimmerman M et al. *Compr Psychiatry.* 2007;48(2):113-117;
3. Fava M. *J Psychopharm.* 2006;20(3):29-34;
4. Paykel ES et al. *Psychol Med*. 1995;25(6):1171-1180;
5. Pintor L et al. *J Affect Disord*. 2004;82(2):291-296;
6. Romera I et al. *BMC Psychiatry*. 2013;13:51.

Remission as Goal of Treatment

- Only approximately 28% of patients treated for MDD achieve remission* following treatment with a single antidepressant[1]
- Partial response (indicated by a 25% to 49% reduction in depressive symptoms) is common[2]
- Patients not achieving a full remission typically suffer from troubling residual symptoms[2]
- Even patients considered to be fully remitted report experiencing at least one residual symptom[3,4]
- Ideally, the goal of treatment for MDD is for patients to achieve full remission[5]

*Remission defined as a score of ≤5 on the Hamilton Depression Rating Scale.

MDD, major depressive disorder.

1. Trivedi MH et al. *Am J Psychiatry*. 2006;163:28-40;
2. Fava M. *J Psychopharm*. 2006;20(3):29-34;
3. Paykel ES et al. *Psychol Med*. 1995;25(6):1171-1180;
4. Nierenberg AA et al. *Psychol Med*. 2010;40(1):41-50;
5. Trivedi M. *Psychiatry Weekly*. May 21, 2007.

Significant Challenges Exist Surrounding the Treatment of MDD

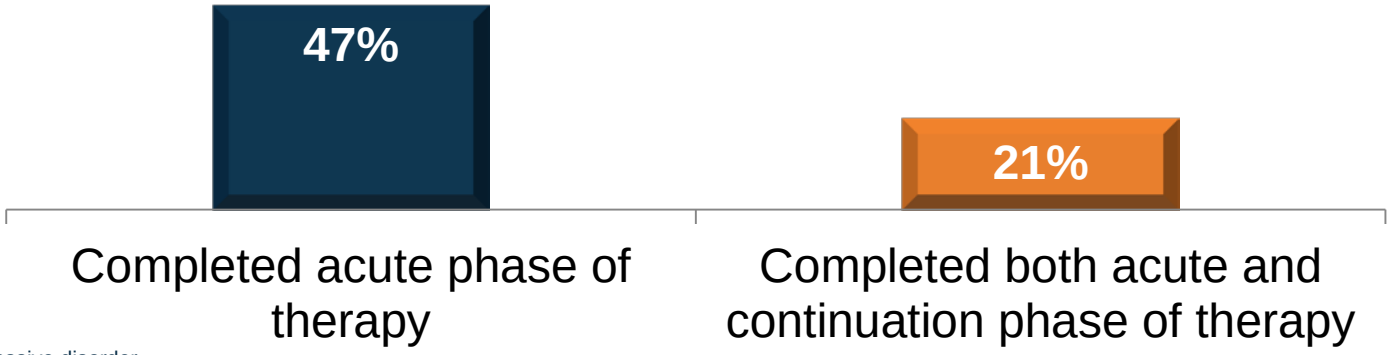
- **There is significant unmet need in the treatment of MDD:**
  - under-treatment due to misdiagnosis or underdiagnosis[1]
  - low rates of adherence and persistence to therapy,[2] potentially influenced by:
    - slow onset of action: antidepressants require 4–6 weeks to achieve full therapeutic effect[3]
    - lack of efficacy: a significant proportion of patients fail to remit or only partially remit despite adequate therapy[4,5]
    - poor tolerability: adverse events associated with pharmacologic agents may reduce adherence and persistence[3]
  - low rates of guideline-concordant follow up[6]

MDD, major depressive disorder.

1. Nierenberg. *Am J Manag Care*. 2001(suppl 11):353-66;
2. Cantrell, et al. *Med Care*. 2006;44(4):300-303;
3. Gelenberg, et al. American Psychiatric Association. Practice guideline for the treatment of patients with major depressive disorder. 2010;
4. Olchanski, et al. *Clin Ther*. 2013;35(4):512-22;
5. Nierenberg, et al. *Psychol Med*. 2010;40(1):41-50;
6. Chen, et al. *Gen Hosp Psych*. 2010;32:360-367.

Adherence to Therapy Is a Key Issue in Treating Patients With MDD

- **The association between prescriber specialty, follow-up visits, and proportion of patients to complete antidepressant regimen was estimated retrospectively using data from a large national health plan (N = 4102)[1]:**
  - overall, less than half of patients completed the acute phase of therapy and approximately only 1/5 completed both the acute and continuation phase[1]
- **These results suggest improved adherence to antidepressants is seen when proper provider support is in place and patients participate in frequent follow-up**



MDD, major depressive disorder.

1. Chen, et al. *Gen Hosp Psych.* 2010;32:360-367.

Urgency to Treat Residual Symptoms

- Residual depressive symptoms are associated with an increased risk of relapse and poor psychosocial functioning[1,2]
- Adequate pharmacological intervention early in the disease is important to reduce the amount of the time in a depressed state, thereby decreasing the risk of suicide[1,2]

1. Fava M. *J Psychopharmacology*. 2006;20(3):29-34.
2. Sokero TP et al. *Br J Psychiatry*. 2005;186:314-318.

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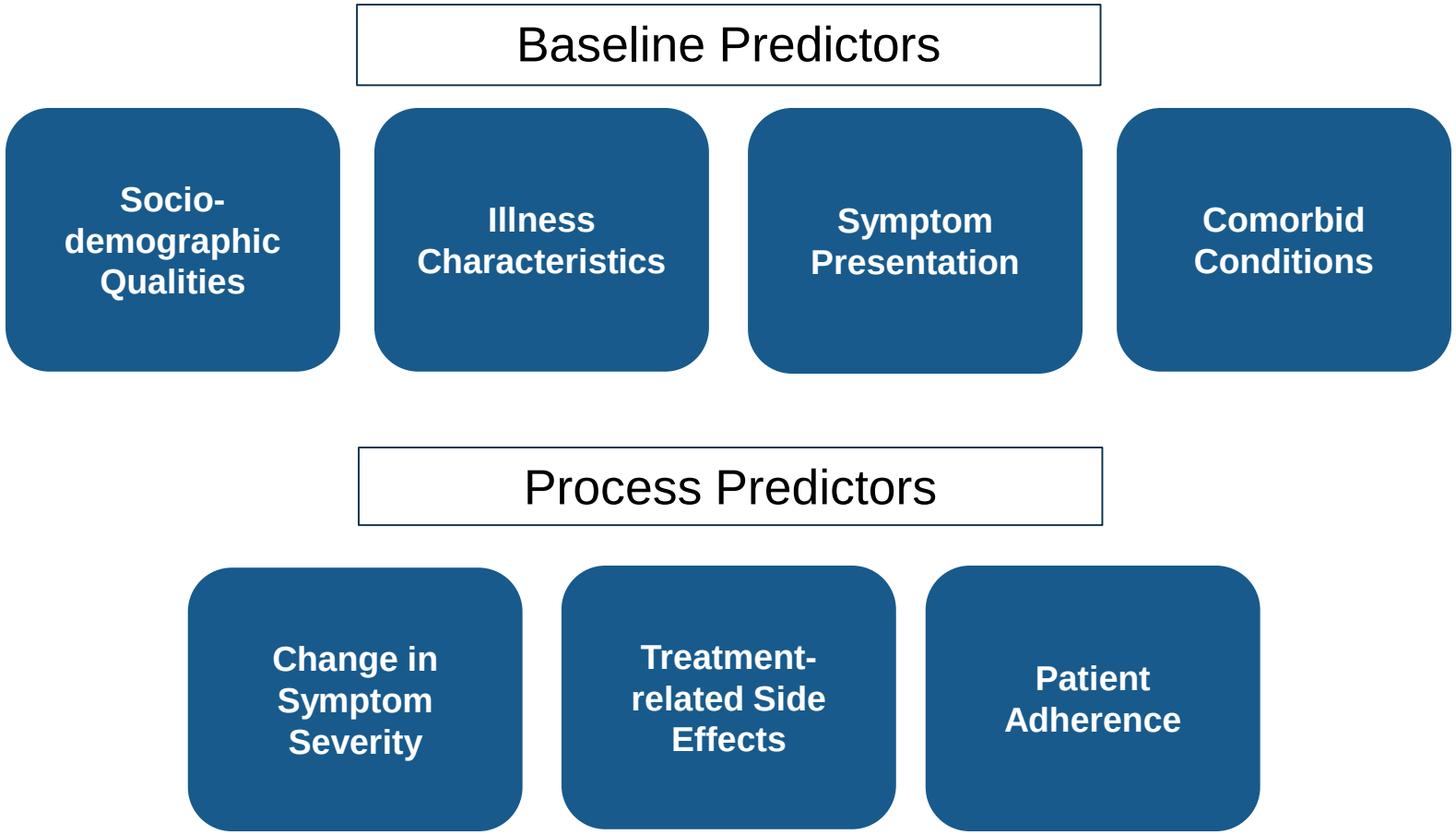
RESPONSE TO ANTIDEPRESSANT TREATMENT IN MDD

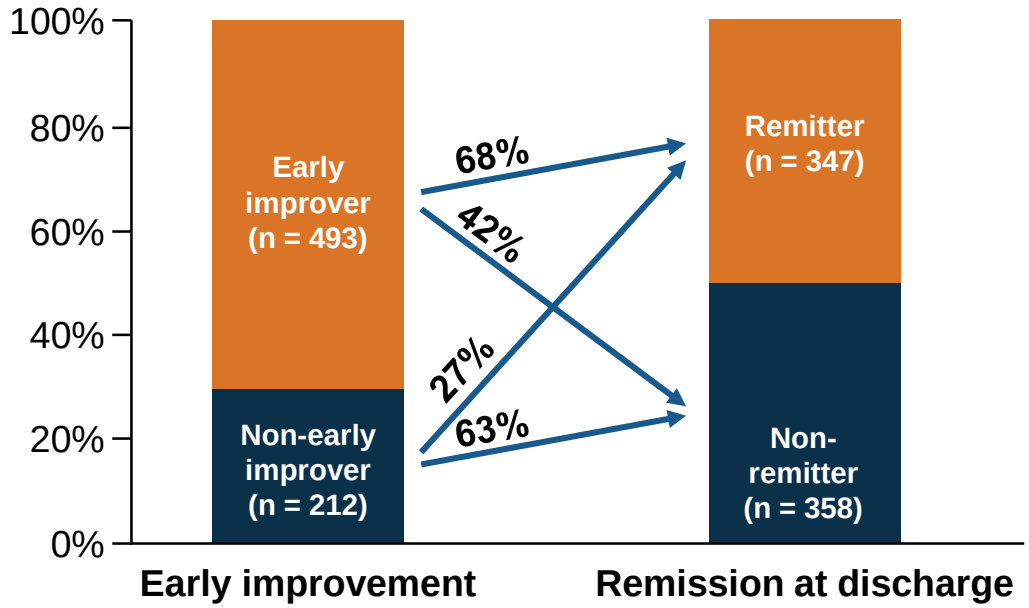
Mary D Moller, DNP, ARNP, PMHCNS-BC, CPRP, FAAN

Predicting Patient Response to Antidepressant Treatment



1. Trivedi M. *Psychiatry Weekly*. May 21, 2007.

Early Improvement Is Common and Predicts Remission



- Earlier onset of response before 2 weeks is common and highly predictive of later outcome[1-3]
- If no improvement is observed after 2 weeks, treatment should be adjusted or changed immediately[4]

1. Henkel V et al. *J Affect Disord*. 2008;115:439-449;
2. Nierenberg AA et al. *Am J Psychiatry*. 1995; 152:1500-1503;
3. Szegedi A et al. *J Clin Psychiatry*. 2009;70:344-353;
4. Möller HJ et al. *Medicographia*. 32;2010:139-145.

Identifying the Inadequately Treated Patient

- Measurement tools for assessing severity of depression used during the first 2–4 weeks of antidepressant treatment can accurately predict the likelihood of a response or lack of response to treatment after a longer term (8 weeks)[1]
- Assessment tools to evaluate changes in symptom states during the first 4 weeks of treatment can also predict treatment response at 12 weeks[2]
  - Dividing the HAM-D-17 into symptom clusters (mood, sleep/psychic anxiety, appetite, and somatic anxiety/weight) and evaluating change scores at 4 weeks correctly assigned up to 70% of patients as late responders or nonresponders at 12 weeks

HAM-D-17, 17-item Hamilton Depression Rating Scale.

1. Nirenberg AA et al. *Am J Psychiatry*. 2000;157:1423-1428;
2. Trivedi MH et al. *J Clin Psychiatry*. 2005;66(8):1064-1070.

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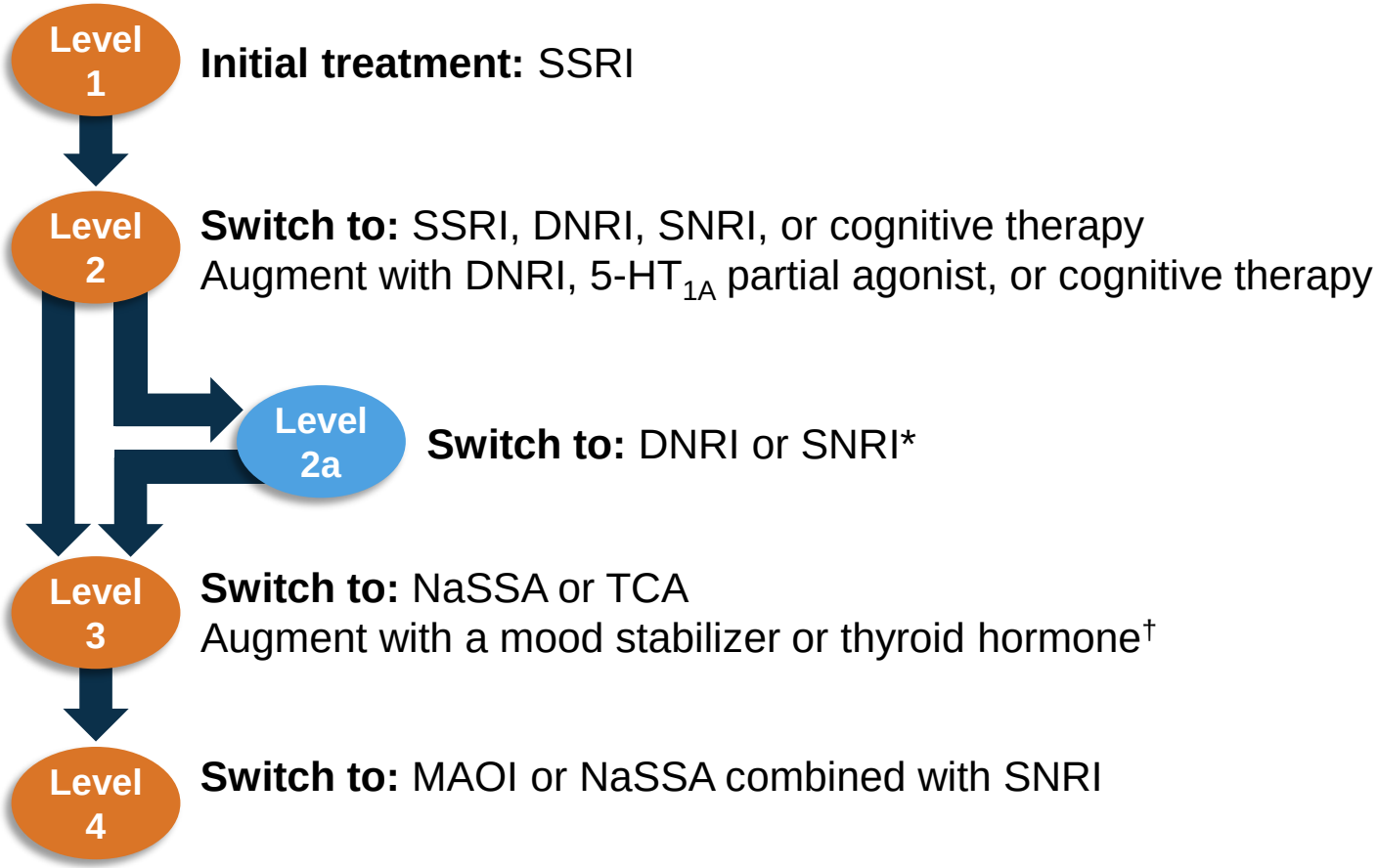
EVIDENCE FOR THE TREATMENT OF PATIENTS WITH MDD AND PRACTICAL GUIDELINES

Georgia Stevens, PhD, APRN, PMHCNS-BC

STAR*D Treatment Algorithm: Examining Different Treatment Strategies in a "Real-world" Setting



*Only for those who failed cognitive therapy; †Only with DNRI, SSRI, or SNRI.

DNRI, dopamine and norepinephrine reuptake inhibitor; MAOI, monoamine oxidase inhibitor; NaSSA, noradrenergic and specific serotonergic antidepressant; SNRI, serotonin norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; STAR*D, Sequenced Treatment Alternatives to Relieve Depression; TCA, tricyclic antidepressant.

1. Rush AJ et al. *Am J Psychiatry.* 2003;160(2):237.

STAR*D Results

Symptom Remission[a] (% Patients)

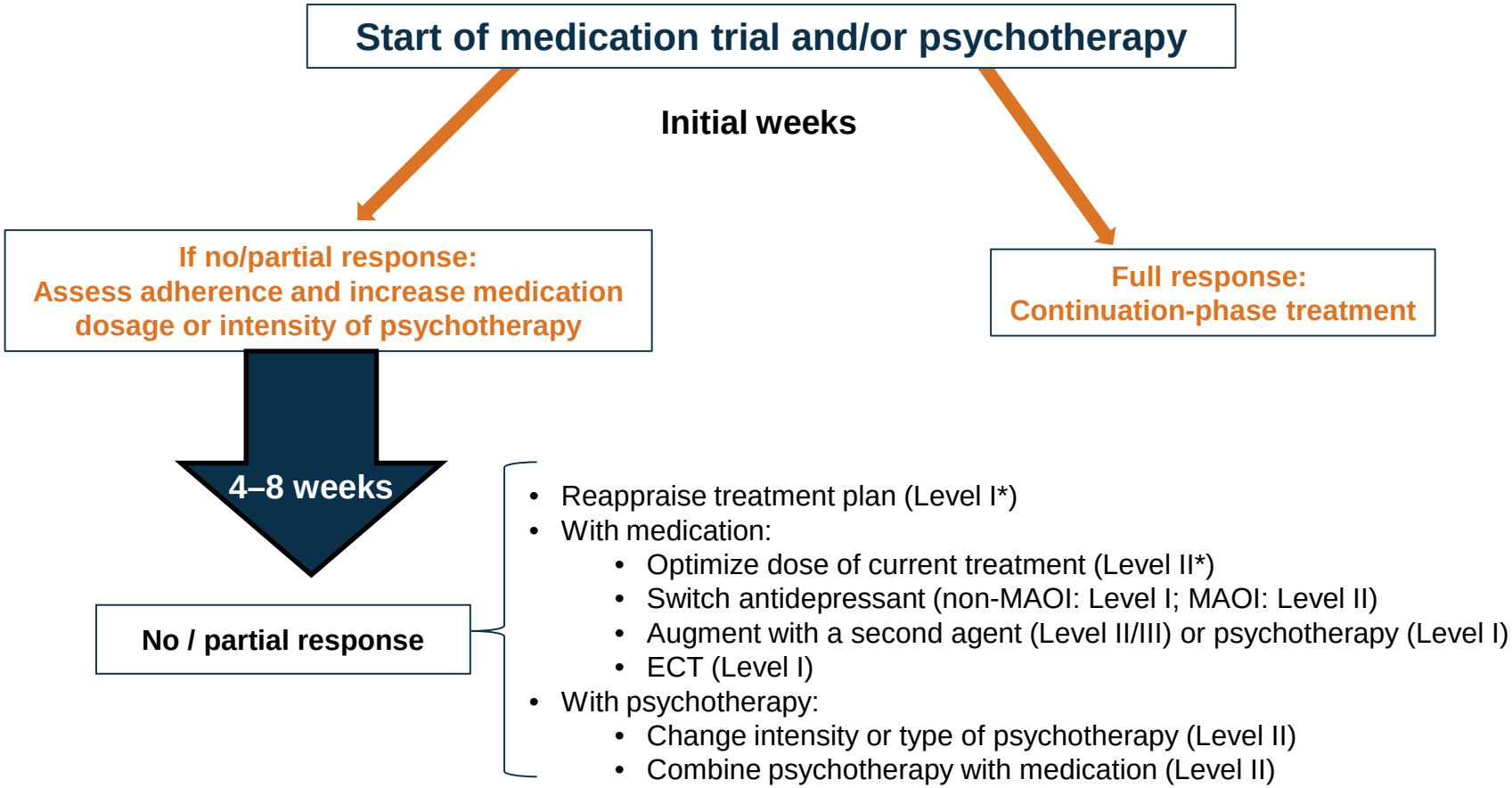
Level 1[1,2]	**SSRI (n = 3671)**				**28%**		
Level 2[3-5]	**SSRI (n = 238)**	**DNRI (n = 239)**	**SNRI (n = 250)**	**Cognitive Therapy (n = 36)**	**DNRI + SSRI (n = 279)**	**5HT-1A Partial Agonist + SSRI (n = 286)**	**Cognitive Therapy + SSRI (n = 65)**
	18%	**21%**	**25%**	**25%**	**30%**	**30%**	**23%**
Level 3[6,7]	**NaSSA (n = 114)**		**TCA (n = 121)**		**Mood Stabilizer +ADT (n = 69)**	**Thyroid Hormone +ADT (n = 73)**	
	12%		**20%**		**16%**	**25%**	
Level 4[8]	**MAOI (n = 58)**		**NaSSA + SNRI (n = 51)**				
	7%		**14%**				

Note: Trial was not designed to directly compare switch or augmentation medication treatments.
[a]Defined by exit score ≤ 7 on the HAM-D-17.

ADT, antidepressant therapy; DNRI, dopamine and norepinephrine reuptake inhibitor; HAM-D-17, 17-item Hamilton Depression Rating Scale; MAOI, monoamine oxidase inhibitor; NaSSA, noradrenergic and specific serotonergic antidepressant; SNRI, serotonin norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; STAR*D, Sequenced Treatment Alternatives to Relieve Depression; TCA, tricyclic antidepressant.

1. Rush AJ et al. Am J Psychiatry. 2006;163:1905-1917;
2. Trivedi MH et al. *Am J Psychiatry*. 2006;163(1):28-40;
3. Rush AJ et al. *N Engl J Med*. 2006;354(12):1231-1242;
4. Thase ME et al. *Am J Psychiatry*. 2007;164(5):739-752;
5. Trivedi MH et al. *N Engl J Med*. 2006;354(12):1243-1252;
6. Fava M et al. *Am J Psychiatry*. 2006;163 (7):1161-1172;
7. Nierenberg AA et al. *Am J Psychiatry*. 2006;163(9):1519-1530;
8. McGrath PT et al. *Am J Psychiatry*. 2006;163(9):1531-1541.

Revised APA Guidelines for the Acute-phase Treatment of MDD



*Level I = recommended with substantial clinical confidence; Level II = recommended with moderate clinical confidence; (Level III = may be recommended on the basis of individual circumstances).

APA, American Psychiatric Association; ECT, electroconvulsive therapy; MAOI, monoamine oxidase inhibitor; MDD, major depressive disorder.

1. Adapted from American Psychiatric Association. Practice Guideline for the Treatment of Patients With Major Depressive Disorder. 3rd ed. Arlington, VA: American Psychiatric Association; 2010.

Revised APA Guidelines: Augmentation Recommendations for No/Partial Response to Antidepressant Therapy

Augmentation Options*	Level of Clinical Confidence (I-III)‡
Psychotherapy	I
Second Antidepressant Therapy†	II
Atypical Antipsychotic	
Thyroid Hormone	
Mood Stabilizer	
Anticonvulsant	III
Psychostimulant	
Omega-3 Fatty Acid	
Folic Acid	
Anxiolytic or Sedative/Hypnotic	

*Classes of medication have been used in this table to replace some of the specific drug names.

†Includes non-MAOI and MAOI antidepressants.

‡Level I = recommended with substantial clinical confidence; Level II = recommended with moderate clinical confidence; (Level III = may be recommended on the basis of individual circumstances).

APA, American Psychiatric Association.

1. Adapted from American Psychiatric Association. Practice Guideline for the Treatment of Patients With Major Depressive Disorder. 3rd ed. Arlington, VA: American Psychiatric Association; 2010.

Nonpharmacologic Therapies for MDD

Categories of Care	Care Strategies
Psychotherapy	Cognitive Behavioral Therapy (CBT)[1]
	Interpersonal Therapy[1]
	Group Therapy[1]
	Problem Solving Therapy[1]
	Future Directed Therapy (FDT)[2]
Alternative Mind-Body Therapy	Relaxation techniques (breathing exercises, meditation, etc)[3]
	Yoga, tai chi, qigong[3]
Family/Caregiver Involvement	Family/caregiver involvement in the patient treatment plan facilitates day to day management of chronic difficulties of depression[4]
Web-Based Intervention	Deprexis (an interactive program that integrates multiple therapeutic approaches to depression)[5]

MDD, major depressive disorder.

1. American Psychiatric Association. Practice Guideline for the Treatment of Patients With Major Depressive Disorder. 3rd ed. Arlington, VA: American Psychiatric Association; 2010.
2. Vilhauer JS et al. *Innov Clin Neurosci*. 2013;10(3):12-2;
3. Bertisch SM et al. *J Psychosom Res*. 2009;66(6):511-519;
4. Justin RG. *Prim Care Companion. J Clin Psychiatry*. 2001;3(6):267;
5. Meyer B et al. *J Med Internet Res*. 2009;11(2):e15.

Challenges and Integrated Care Strategies for MDD

- Patient is feeling somewhat better following antidepressant treatment initiation but complains of lingering feelings of depressed mood
- Patient is feeling better with antidepressant therapy but complains of insomnia or aches and pains
- Patient is in obvious need of social support but is not interested in, or does not have access to, help (such as a support group)
- Patient complains that family members do not understand what they are going through and think family members are just angry and frustrated with them
- Patient is partially responding to antidepressant but expresses feelings of hopelessness and a general low satisfaction with life

MDD, major depressive disorder.

Measurement-based Care

- Among practitioners, clinical treatment of depression is often associated with wide variations in dosage and duration of treatment[1]
- Measurement-based care was developed as a systematic approach to evaluate patient progress and eliminate variability in patient treatment among physicians
  - In STAR*D, measurement-based care included the routine measurement of symptoms and side effects at each treatment visit; a treatment manual was used by treating physicians that detailed precisely when and how to modify medication regimens or doses based on results of assessments[2]
- A wide variety of physician-rated and patient-rated scales are currently available to evaluate patient symptoms, functioning ability, treatment progress, and side effects[3]
  - For more information, please see: http://www.outcometracker.org/scales_library.php

STAR*D, Sequenced Treatment Alternatives to Relieve Depression.

1. Trivedi MH et al. *Neuropsychopharmacology*. 2007;32(12):2479-2489.;
2. Trivedi MH et al. *Am J Psychiatry*. 2006;163(1):28-40;
3. Zimmerman M. http://www.outcometracker.org/scales_library.php. Accessed October 1, 2013.

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Summary

- MDD is a serious, chronic, disabling illness affecting hundreds of millions of individuals worldwide
- Use of assessment tools and measurement-based care may facilitate patient-physician dialogue
- Residual symptoms are common and cause significant psychosocial and occupational functional impairment
- Over 90% of MDD patients experience residual symptoms during the course of treatment
  - These patients are at increased risk for depressive relapse
- Patients with residual symptoms, relapse, and/or suicidality should receive increased vigilance and a more aggressive treatment approach (including combination therapy, psychotherapy, cognitive behavioral therapy, etc)

MDD, major depressive disorder.

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