



IMPROVING OUTCOMES FOR PRIMARY CARE PATIENTS WITH DEPRESSION

Rakesh Jain, MD, MPH; W. Clay Jackson, MD, DipTh; and C. Brendan Montano, MD

This activity is derived from the planning teleconference series “Strategies to Improve Outcomes for Primary Care Patients With Major Depressive Disorder,” which was held on February 5, 2015. This report was prepared and independently developed by the CME Institute of Physicians Postgraduate Press, Inc., and was supported by an educational grant from Takeda Pharmaceuticals International, Inc., U.S. Region and Lundbeck.

The teleconference was chaired by **Rakesh Jain, MD, MPH**, Department of Psychiatry, Texas Tech University Health Sciences Center School of Medicine, Permian Basin. The faculty were **W. Clay Jackson, MD, DipTh**, Departments of Family Medicine and Psychiatry, University of Tennessee College of Medicine, Memphis; and **C. Brendan Montano, MD**, Connecticut Clinical Research, Cromwell.

Financial disclosure: Dr Jain is a consultant and paid speaker for Addrenex, Forest, Eli Lilly, Lundbeck, Merck, Otsuka, Pamlab, Pfizer, Shionogi, Shire, Sunovion, and Takeda; is a member of the advisory boards for Addrenex, Eli Lilly, Lundbeck, Merck, Otsuka, Pamlab, Pfizer, Shionogi, Shire, Sunovion, and Takeda; and has received research support from AstraZeneca, Forest, Eli Lilly, Lundbeck, Otsuka, Pfizer, Shire, and Takeda. Dr Jackson is a consultant for DepoMed, Pamlab, and Sunovion; has received honoraria from Otsuka; and is a member of the speakers bureaus for Pamlab and Sunovion. Dr Montano is a consultant for and has received honoraria from Takeda, Lundbeck, Otsuka, Shire, and Merck and is a member of the speakers/advisory boards for Takeda, Lundbeck, Shire, Merck, Actavis, and Sunovion.

The opinions expressed herein are those of the faculty and do not necessarily reflect the opinions of the CME provider and publisher or the commercial supporter.

Prim Care Companion CNS Disord
2015;17(6):doi:10.4088/PCC.14061n17c

© Copyright 2015
Physicians Postgraduate Press, Inc.

Primary care physicians (PCP) treat many patients with depression but may be less likely than specialists to provide measurement-based care. Optimal care for major depressive disorder (MDD) should involve regular assessment of symptom resolution, treatment adherence, and tolerability. The following 3 case presentations demonstrate how measurement-based care can be used to monitor treatment benefits and adverse effects, how to improve adherence and patient outcomes, and how to recognize and treat residual symptoms. To listen to podcast discussions of the cases among faculty experts, go to PSYCHIATRIST.COM and enter the keyword *depression*.

THE BENEFITS OF MEASUREMENT-BASED CARE FOR PRIMARY CARE PATIENTS WITH DEPRESSION

W. Clay Jackson, MD, DipTh

Measurement-based care provides many benefits for clinicians who are managing patients with MDD and is recommended by American Psychiatric Association (APA) practice guidelines.¹ Regular use of measurements can improve patient outcomes. For example, a study² of 915 primary care patients found that remission and response rates at 6 months were higher for patients whose severity was scored monthly than for the control group, who were assessed at 6 months.

Rating scales and symptom screeners such as the 9-item Patient Health Questionnaire (PHQ-9), Generalized Anxiety Disorder scale (GAD-7), Mood Disorder Questionnaire (MDQ), and World Health Organization well-being index (WHO-5) can be quickly and easily completed by patients before or during their visits and can provide additional information that may guide treatment decisions. The PHQ-9 assesses the frequency of the 9 MDD criteria in the *Diagnostic and Statistical Manual of Mental Disorders (DSM)*, while the GAD-7 assesses the frequency of 7 common anxiety symptoms. The MDQ is a screening tool for bipolar disorder, and the WHO-5 is a questionnaire covering 5 items related to well-being.

To access the rating scales in this activity, visit these websites:

- <http://www.integration.samhsa.gov/clinical-practice/screening-tools> (PHQ-9, MDQ, AUDIT, CAGE-AID, GAD-7)
- <http://www.karger.com/Article/FullText/376585> (WHO-5)
- <http://psycheducation.org/primary-care-provider-resource-center/moodcheck> (MoodCheck)
- <http://www.hcp.med.harvard.edu/ncs/asrs.php> (ASRS)

CASE PRESENTATION

The following case of Mrs C illustrates how rating scales may be used in a patient's care.
Initial visit. Mrs C is a 38-year-old patient who presented to her clinician with symptoms including trouble sleeping, tearfulness, depressed mood, irritability, and anxiety. She had a postpartum depressive episode 11 years ago, which was successfully treated with sertraline, although she could not remember the dose. At this initial visit, she resumed sertraline treatment at 50 mg/d for MDD.

Follow-up visit. At her 1-month follow-up visit, Mrs C was still losing sleep and was tearful and anxious. When asked about work, she reported missing 4 days and was fearful of losing her job due to absenteeism. Her clinician administered several screening instruments at this visit. She had a PHQ-9 score of 16, a GAD-7 score of 13, a WHO-5 score of 8, and a negative MDQ screen. Each of these scales was used to aid the clinician's understanding of Mrs C's diagnosis, treatment response, and quality of life.

“Eleven years ago, I don't think many of us were thinking about quantitative metrics in practice. But today, I think that's an evolving standard of care.”

—Dr Jackson

CONFIRM THE DIAGNOSIS

Because Mrs C did not respond well to treatment and because postpartum depression can be associated with bipolar disorder,³ her clinician should consider that the initial diagnosis of MDD may be incorrect. The negative MDQ score increases the likelihood that Mrs C does not have bipolar disorder, but it is not enough to rule out that diagnosis. Clinicians should inquire about substance abuse, other mood disorders, and suicidality, which are common in patients with bipolar disorder and in their family history.^{4,5} Other red flags for bipolar disorder include irritability and anxiety.⁶ These symptoms should be monitored to see if they improve with antidepressant treatment.

The GAD-7 is useful to screen for anxiety symptoms, which are often present with both MDD and bipolar disorder.⁷ Patients with major depressive episodes frequently have comorbid anxiety disorders. Anxiety symptoms must be treated because they can significantly influence MDD outcomes. For example, comorbid anxiety causes more functional impairment, greater suicide risk, and slower response to medication than in patients with depression alone.⁷ While rating scales by themselves cannot diagnose MDD, bipolar disorder, or anxiety disorders, they are useful tools to guide the clinician-led interview for more information to confirm a diagnosis.

TRACK TREATMENT RESPONSE

In Mrs C's case, follow-up occurred after 1 month of taking sertraline at 50 mg/d. An earlier follow-up, at 2 or 3 weeks, may have been beneficial so that the clinician could gauge the lack of improvement sooner. Another reason for faster follow-up is for clinicians to ensure that patients are taking their medication and not experiencing significant adverse effects. Many patients who are prescribed an antidepressant fail to fill their prescriptions or stop taking their medications in the first month.^{8,9} Therefore, having some contact with patients before a month has passed, even a telephone call from a nurse or office professional, may help patients with adherence.¹⁰ In this case, Mrs C reports relatively good adherence, missing only 2 doses in the past month.

Although Mrs C was not given the PHQ-9 or other screening instruments at her first visit for comparison, her PHQ-9 score of 16 at her follow-up visit indicates moderate to moderately severe

depression, while her GAD-7 score of 13 indicates moderate anxiety. Thus, her rating scale scores demonstrate that she is not responding to treatment. At this point, her clinician may consider strategies such as increasing the antidepressant dose, switching to another antidepressant, or augmenting the antidepressant.¹ The initial medication for MDD should be administered at an adequate dose for an adequate duration, usually 4 to 8 weeks.¹ If Mrs C's sertraline dose is increased and she still shows no response, other strategies should be considered.

Augmentation strategies, such as with an atypical antipsychotic, may be used for patients who show partial response to initial treatment.¹ However, for a patient who shows no response, the best strategy may be switching to another medication.¹ One consideration when switching medications is the agent's mechanism of action. Although patients can be switched to an agent within the same class, such as from one selective serotonin reuptake inhibitor (SSRI) to another SSRI, some patients may benefit from switching from an SSRI to a serotonin-norepinephrine reuptake inhibitor (SNRI) or to an agent with multiple mechanisms of action.¹

“We worry a lot about the drugs, but sometimes it is duration and dose that are the challenge.”

—Dr Jackson

DETERMINE QUALITY OF LIFE

In addition to the goal of helping Mrs C respond to treatment and attain remission (a PHQ-9 score of 4 or less), the clinician also wants to improve her sense of well-being, which means reaching a WHO-5 score of at least 13. Nonpharmacologic interventions, such as cognitive-behavioral therapy (CBT), interpersonal psychotherapy (IPT), or mindfulness-based cognitive therapy (MBCT), may be used at any time throughout treatment,¹ but their use depends on cost, availability, and patient preference. Additionally, Mrs C may not be able to take full advantage of psychotherapy until her symptoms improve and she feels a bit better. In a study¹¹ of patients with recurrent depression, MBCT was more effective than maintenance-phase antidepressants in reducing depressive symptoms and improving quality of life. Relapse rates were 47% for the MBCT group compared with 60% for the maintenance antidepressant group.

Exercise is another effective intervention for some patients with depression, often used to augment medication or psychotherapy.^{1,12} Exercise can help restore patients' feelings of wellness and improve overall health.

Quality of life is determined not just by living without symptoms of depression but also by experiencing satisfaction with life, good-quality relationships, and positive emotions (Table 1).¹³ Therapies such as MBCT and exercise can be used to increase these positive feelings rather than to target symptoms of depression the way pharmacologic interventions do. Formal psychotherapies, such as positive psychology or positive psychotherapy, are being developed that help people recognize and augment their internal strengths to enhance wellness.¹⁴

Leaving patients with an inadequate response to treatment without attempting more sophisticated management strategies is unacceptable. Using rating scales is one way for clinicians to ensure

Table 1. Elements of Well-Being^a

- Presence of positive emotions (eg, contentment, happiness)
- Absence of negative emotions (eg, depression, anxiety)
- Satisfaction with life
- Fulfillment
- Positive functioning

^aBased on Centers for Disease Control and Prevention.¹³

they recognize patients' poor response so that they can adjust treatment as necessary to eventually achieve remission and improve well-being in their patients.

CONCLUSION

As the case of Mrs C demonstrates, many patients have an insufficient response to initial antidepressant treatment. Clinicians can use rating scales at baseline and follow-up visits to help confirm a diagnosis, track symptoms, and understand patients' well-being. When patients demonstrate a partial or inadequate response to treatment, clinicians should reassess the initial diagnosis and any comorbid illnesses, address adherence and adverse effects, and then adjust treatment accordingly. Strategies for treating suboptimal response include maximizing the antidepressant dose, augmenting the antidepressant, or switching to another medication. Nonpharmacologic treatment options including CBT, IPT, MBCT, and exercise may be useful as primary or adjunctive therapies, depending on the severity of depression and patient preference. In the case of Mrs C, rating scale results helped alert the clinician that she was not progressing to remission and thus needed treatment adjustments.

Drug name: sertraline (Zoloft and others)

REFERENCES

1. Gelenberg AJ, Freeman MP, Markowitz JC, et al. *Practice Guideline for the Treatment of Patients With Major Depressive Disorder*. Arlington, VA: American Psychiatric Association; 2010.
2. Yeung AS, Jing Y, Brennenman SK, et al. Clinical Outcomes in Measurement-based Treatment

Clinical Points

- ▶ Use a rating scale such as the PHQ-9 or MDQ to help confirm a diagnosis of MDD or bipolar disorder
- ▶ Continue to monitor symptoms throughout treatment using rating scales like the PHQ-9 and GAD-7
- ▶ Consider using psychotherapy (eg, CBT, IPT, MBCT, positive psychotherapy) and exercise to help patients improve their sense of well-being, which can be rated with the WHO-5

(Comet): a trial of depression monitoring and feedback to primary care physicians. *Depress Anxiety*. 2012;29(10):865–873.

3. National Alliance on Mental Illness. Pregnancy and bipolar disorder: fact sheet. http://www2.nami.org/factsheets/pregnancybipolar_factsheet.pdf. Reviewed July 2013. Accessed October 20, 2015.
4. Tondo L, Visioli C, Preti A, et al. Bipolar disorders following initial depression: modeling predictive clinical factors. *J Affect Disord*. 2014;167:44–49.
5. Serretti A, Chiesa A, Calati R, et al. Influence of family history of major depression, bipolar disorder, and suicide on clinical features in patients with major depression and bipolar disorder. *Eur Arch Psychiatry Clin Neurosci*. 2013;263(2):93–103.
6. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington, VA: American Psychiatric Association; 2013.
7. Kornstein SG, Schneider RK. Clinical features of treatment-resistant depression. *J Clin Psychiatry*. 2001;62(suppl 16):18–25.
8. Sansone RA, Sansone LA. Antidepressant adherence: are patients taking their medications? *Innov Clin Neurosci*. 2012;9(5-6):41–46.
9. Demyttenaere K. Risk factors and predictors of compliance in depression. *Eur Neuropsychopharmacol*. 2003;13(suppl 3):S69–S75.
10. Solberg LI, Trangle MA, Wineman AP. Follow-up and follow-through of depressed patients in primary care: the critical missing components of quality care. *J Am Board Fam Pract*. 2005;18(6):520–527.
11. Kuyken W, Byford S, Taylor RS, et al. Mindfulness-based cognitive therapy to prevent relapse in recurrent depression. *J Consult Clin Psychol*. 2008;76(6):966–978.
12. Mura G, Moro MF, Patten SB, et al. Exercise as an add-on strategy for the treatment of major depressive disorder: a systematic review. *CNS Spectr*. 2014;19(6):496–508.
13. Centers for Disease Control and Prevention (CDC). Health-Related Quality of Life (HRQL): Well-being concepts. <http://www.cdc.gov/hrqol/wellbeing.htm>. Updated March 6, 2013. Accessed October 20, 2015.
14. Schrank B, Brownell T, Tylee A, et al. Positive psychology: an approach to supporting recovery in mental illness. *East Asian Arch Psychiatry*. 2014;24(3):95–103.

TACTICS TO IMPROVE ADHERENCE IN DEPRESSED PRIMARY CARE PATIENTS

C. Brendan Montano, MD

Many patients diagnosed with depressive disorders are not well educated about the importance of treatment adherence. Since nonadherence or partial adherence is a serious problem, clinicians should carefully explain the treatment regimen during initial visits, monitor adherence during acute treatment, and reinforce treatment instructions throughout continuation and maintenance treatment phases. The case of Mr K illustrates useful tools to educate patients on why adherence is important and highlights some of the major reasons why patients may not follow treatment instructions.

CASE PRESENTATION

Initial visit. Mr K is a 28-year-old patient who visited his PCP after feeling depressed for the past few months. He had no previous history of depression, and his clinician administered several screening instruments during this visit. Mr K had a PHQ-9 score of 22 out of 27,

which indicates severe depression, and his MDQ screen was negative for bipolar disorder, with a score of 6 out of 13. Mr K admitted that he was worried about having recently lost his job and hoped that he would increase his chances for finding a new position if he improved his emotional well-being. His clinician prescribed the SSRI citalopram at a dose of 20 mg/d for MDD.

Follow-up visit. Mr K was late for his 1-month follow-up visit and was noticeably irritable with the office staff. He stated that he had been

“Even in patients who are well insured and who can afford their medication, as many as 15 to 20 percent . . . don’t even fill their first prescription.”
—Dr Jain

taking his medication as indicated, although sometimes he forgot. He believed he had been experiencing less anxiety, and his PHQ-9 score had decreased 4 points since his initial visit. However, when asked about treatment side effects, Mr K admitted that he intentionally did not take his medication on the weekends because it caused sexual dysfunction. Additionally, he reported that he had been arrested for driving while intoxicated (DWI) since his last visit, and he was concerned about his impending court date and the potential loss of his driver's license.

DETERMINE REASONS FOR NONADHERENCE

Mr K's case demonstrates 2 common reasons for patient nonadherence: adverse effects of medication and forgetfulness. Other reasons include poor clinician-patient communication, inadequate education about the drug and the most effective ways to take it, not believing that medication is needed, and cost.¹

"I tell them [patients] if they don't take the full doses as long as it's recommended that they are at risk of having recurrence and at risk of having worsening depression over time."

—Dr Montano

Some patients stop taking medication because they believe they are doing better and no longer need it.¹ Other patients may not even fill their first prescription.² A study² of pharmacy data for electronic antidepressant prescriptions found that individuals with new antidepressant prescriptions were 5 times more likely to not pick them up than users who had been prescribed antidepressants in the past. Patients aged 18–34 years were the most likely to have unfilled prescriptions.² More than one-fourth of patients stop their antidepressants without their doctors' consent by the end of the first month, and 44% stop by the third month.³

Clinicians should consider several questions to determine a course of action once the patient's reason for nonadherence is clear. In Mr K's case, does he need more education about the benefits of his medication and encouragement to continue it with full adherence so that his response to an adequate trial can be observed? Should he be switched to another antidepressant since his PHQ-9 score decreased only a small amount and an antidepressant in another class might lessen the sexual dysfunction?⁴ Most importantly, is the initial diagnosis of depression correct?

CONFIRM THE DIAGNOSIS

Mr K scored high on the PHQ-9 and received a negative score on the MDQ assessment for bipolar disorder, which led his clinician to diagnose him with MDD. Although his MDQ score was negative, 6 is just barely negative; 7 is positive for bipolar disorder. In addition to asking the number of symptoms, the MDQ also asks about impairment (with work, money, family, the law) due to the symptoms endorsed, and Mr K had checked "minor" for his level of problems. However, his clinician should consider whether Mr K's symptoms and their severity were initially underreported. The fact that Mr K has lost his job and gotten into legal trouble indicates moderate or serious problems. Questioning Mr K further to assess for bipolar

disorder, as well as attention-deficit/hyperactivity disorder (ADHD) and substance use disorder, would be useful. Clinicians may also be able to collect helpful data by questioning their patients' family members and close friends for a more comprehensive report.

Bipolar disorder. Signs that Mr K may have entered a hypomanic or manic state after starting the antidepressant include his irritability with the office staff on his follow-up visit and risky behavior as evidenced by his recent DWI.⁵

When faced with the possibility of a new diagnosis, clinicians should use additional screening tools. To further assess Mr K for bipolar disorder, the MoodCheck assessment tool could be useful because it incorporates aspects of the Bipolar Spectrum Diagnostic Scale and also screens for risk factors such as family history, age at onset, and response to previous antidepressants.

ADHD. The clinician should also take into account that Mr K may have ADHD because it is associated with irritability, occupational instability, and traffic accidents and violations.⁵ Since ADHD begins in childhood and Mr K may not recall his past symptoms, his clinician should ask him to allow the use of collateral information from family members. The Adult ADHD Self-Report Scale (ASRS) can help with the diagnosis, although parental input is most important.

Substance use disorder. As a result of the DWI, the clinician should assess Mr K's level of substance use. Useful screening instruments, such as the Alcohol Use Disorders Identification Test (AUDIT) or CAGE Questionnaire Adapted to Include Drugs (CAGE-AID), may be used to determine if further alcohol or drug assessment is needed.

IMPROVE PATIENT ADHERENCE

Whether Mr K has MDD, bipolar disorder, or ADHD, medication will be part of his treatment regimen. The responsibility falls upon clinicians to thoroughly educate their patients on the necessity of adhering to treatment and on the risks associated with ceasing medications abruptly. Research suggests that as many as 60% of patients cannot accurately describe the specific instructions that their physicians gave them after leaving their office.¹ After describing medication instructions, clinicians can ask patients to tell them what they heard. Clinicians should also warn patients about potential adverse effects and what to do if they experience them. Additionally, they should explain that these medications should not be stopped when patients begin to feel better, unlike, for example, medications taken as needed for cold symptoms.

At each follow-up visit, clinicians should ask about adherence. Most patients want to avoid being chastised by their clinicians when asked if they have been taking their medications. Therefore, if the clinician poses the question in a "yes" or "no" format, the patient will likely respond affirmatively. By changing the way that questions are posed so that they normalize nonadherence, clinicians may be able to gather more accurate information. One effective way to do this is to ask questions such as "How many dosages of your medication have you missed this month?"

To combat forgetfulness, clinicians may suggest that patients place their medications in an area of their house that they will pass by frequently and set a daily phone alarm as a helpful reminder. Research suggests that when clinicians stress the importance of adherence through clear and concise instructions, their patients show a higher rate of compliance (Figure 1).³

Figure 1. Education to Increase Medication Adherence^a



^aBased on Lin et al.³

CONCLUSION

Patients like Mr K who do not fully understand the importance of compliance with medication therapy are at risk for prolonging their depressive symptoms and experiencing more consequences of their illness. Clinicians must take an active role in explaining the importance of medication adherence because patients who are newly diagnosed or do not have a clear understanding of their

treatment regimen may not fill their prescription or may discontinue their medications without their clinicians’ consent or knowledge. If patients have been adherent and are still not responding adequately to treatment, clinicians should reexamine the initial diagnosis by obtaining information from rating scales and collateral reports to further assess symptoms and severity. Finally, clinicians must ensure that patients understand the benefits and adverse effects of their medication and recommend strategies to combat forgetfulness and other reasons that contribute to nonadherence.

Clinical Points

- ▶ Question patients on their medication adherence by normalizing missed doses
- ▶ Collect information from patients’ family and friends to further assess symptom severity and impairment
- ▶ Provide patients with clear instructions on how to use their treatment and what to expect

Drug name: citalopram (Celexa and others)

REFERENCES

1. Jimmy B, Jose J. Patient medication adherence: measures in daily practice. *Oman Med J.* 2011;26(3):155–159.
2. Xing S, Dipaula BA, Lee HY, et al. Failure to fill electronically prescribed antidepressant medications: a retrospective study. *Prim Care Companion CNS Disord.* 2011;13(1):e1–e7.
3. Lin EH, Von Korff M, Katon W, et al. The role of the primary care physician in patients’ adherence to antidepressant therapy. *Med Care.* 1995;33(1):67–74.
4. Clayton AH, El Haddad S, Iluonakhame JP, et al. Sexual dysfunction associated with major depressive disorder and antidepressant treatment. *Expert Opin Drug Saf.* 2014;13(10):1361–1374.
5. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders.* 5th ed. Arlington, VA: American Psychiatric Association; 2013.

THE IDENTIFICATION AND RESOLUTION OF RESIDUAL SYMPTOMS IN DEPRESSED PRIMARY CARE PATIENTS

Rakesh Jain, MD, MPH

CASE PRESENTATION

The following case of Mrs J provides useful steps for identifying and treating residual symptoms in patients with depression.

Initial visit. Mrs J is an 86-year-old woman who visited her PCP complaining of chronic insomnia. She requested the benzodiazepine alprazolam for sleep because it had worked for her sister. Mrs J has a 15-year history of recurrent depression and for which she has been taking an SNRI. She denied having depressive symptoms at this visit and reported that she does not nap during the day. She has no history of excessive snoring or apneic episodes. Mrs J is not overweight, having a current body mass index score of 23. She has hypertension, which is well controlled, and a history of back pain, which has benefited from a recent spinal procedure. Her PCP referred her to a psychiatrist to evaluate her insomnia and to determine if her request for a benzodiazepine is appropriate.

Referral visit. Mrs J and her husband both attend her appointment with a psychiatrist. Her PHQ-9 score of 8 shows mild depressive symptoms, but she insists that she is doing pretty well. However, her

husband disagrees with his wife’s assessment and describes her as having decreased social activity compared with her usual self, significant moodiness, irritability, anger, and some trouble with concentration and fatigue. When questioned further by the psychiatrist, Mrs J agrees that these symptoms are not like her, and they appear to be symptoms of depression that have not fully resolved.

As Mrs J demonstrates, patients with residual symptoms may not recognize that their symptoms are related to their depression. Before clinicians proceed with targeted treatment strategies, they may use a combination of 3 approaches to identify symptoms in patients with depression.

APPROACHES TO SYMPTOM IDENTIFICATION

Question the patient. Mrs J’s primary complaint is insomnia, which is a common symptom in many sleep disorders and medical and psychiatric conditions. The PCP examined snoring, apneic episodes, and weight to rule out obstructive sleep apnea (OSA). The next line of questioning would examine her sleep behaviors. Mrs J told the

PCP that she does not nap in the daytime, but she should be asked whether she drinks caffeinated beverages close to bedtime or has other poor sleep hygiene habits. If these responses are negative, her unresolved depression is likely the cause of her insomnia because the PCP ruled out contributory medical conditions. While her weight does not put her at risk for sleep apnea, hypertension might,¹ but Mrs J's hypertension is under control. Her back pain has resolved and is not keeping her awake at night.

An important topic about which to ask patients with residual symptoms of depression is their medication adherence. Is Mrs J taking her SNRI according to the instructions? Is she taking the full dose? As part of an elderly couple on a fixed income, she may be trying to save money by not filling her prescription regularly.

Use rating scales and screeners. By administering the PHQ-9 at her visit, the psychiatrist was able to recognize that Mrs J was experiencing more symptoms than just insomnia. Using rating scales at every visit is helpful to track patient progress over time, and the results can be reviewed with patients to encourage their involvement. While Mrs J's PHQ-9 results were influenced by her opinion that she was doing well, it still caught some symptoms that otherwise may have gone undetected. It would have been even more helpful if the psychiatrist had been able to compare her PHQ-9 score with a baseline score from the PCP.

Another useful screener is the Epworth Sleepiness Scale, an 8-item questionnaire that asks patients to rate how likely they would be to doze off in activities of daily living.² Higher scores (>10) on the Epworth Sleepiness Scale can direct the clinician to investigate sleep disorders (eg, OSA, narcolepsy), medical conditions (eg, hypertension, obesity), and psychiatric conditions (eg, depression, anxiety) that may cause or contribute to sleep problems.

Collect collateral information. In Mrs J's case, her husband is an excellent source of information. Because Mrs J's other symptoms were less noticeable to her than her insomnia, her husband's report was essential to the assessment. Only after he identified her symptoms of social withdrawal, moodiness, impaired concentration, and fatigue was the psychiatrist able to follow up with questioning to confirm these symptoms. Mr J compared her current behavior with what she is normally like. He was also able to confirm information about her sleep habits, such as the absence of daytime naps and excessive snoring or breathing episodes during the night. Bed partners can help clinicians get a more accurate assessment of patients' sleep habits and overall symptoms, as Mrs J's husband did.

TREATMENT STRATEGIES FOR RESIDUAL DEPRESSIVE SYMPTOMS

Mrs J requested a benzodiazepine for her insomnia, but this strategy is inappropriate for several reasons. First, treating just one symptom (insomnia) does not address her other depressive symptoms, which are likely causing her sleep problems. Second, the efficacy of adjunctive benzodiazepines with SSRIs or SNRIs for depression is not strong, and benzodiazepines carry the risk of dependence and accidents.³ Third, benzodiazepines increase the risk of cognitive dysfunction and falls in elderly patients.⁴ In fact, the American Geriatrics Society Updated Beers Criteria⁴ for potentially inappropriate medication use in older adults gives a strong recommendation *against* the use of benzodiazepines for treatment of insomnia.⁴ By explaining these reasons to Mrs J and

her husband, the psychiatrist can help them understand the risks and direct them to more appropriate treatment options.

Pharmacologic strategies. The first step in resolving residual depressive symptoms is to ensure that the patient's current medication dose is optimized.⁵ An increased dose of the SNRI might alleviate Mrs J's symptoms. However, her age and overall health must be taken into account. For example, if Mrs J has compromised renal function, then optimizing the dose may be inappropriate.⁶ Adverse effects must be carefully monitored regardless of age. Next, the clinician should consider whether other medications may be interfering with antidepressant efficacy or causing depressive symptoms. For example, antihypertensive medications are known to cause depression.⁷ Elderly patients tend to have long medication lists, and one medication or more could be increasing metabolism in the liver or interfering with antidepressant levels.

If the medication dose is maximized and no other medications are found to be interfering, the clinician may choose to augment the current medication or switch treatments.⁵ For patients who are partial responders, augmentation strategies include lithium, atypical antipsychotics (eg, aripiprazole, quetiapine), or a natural product such as L-methylfolate.⁵ While atypical antipsychotics have been used off-label for psychotic symptoms or treatment resistance in patients with depression, they should be considered after other psychotropic drugs or psychotherapies in elderly patients because of their risk of side effects such as stroke and mortality.^{4,8} If atypical antipsychotics are justified based on individual assessment, clinicians must ensure the use of the lowest effective dosage for the shortest time period, balance risks and benefits, and monitor adverse effects including cardiac and metabolic problems.⁸

Combining antidepressants with different mechanisms of action is another strategy that can enhance efficacy or target adverse effects.⁹ Other strategies for treatment-resistant depression include augmenting with buspirone or bupropion or adding cognitive therapy.^{5,9}

Nonpharmacologic strategies. The addition of nonpharmacologic treatments such as IPT and CBT to antidepressants has increased remission rates in patients with resistant and partially responsive depression.⁹

"There is good evidence to show that many of our nonpharmacologic interventions have an explicable biologic mechanism of changing the brain structure and function that we observe to be negatively affected by depression."

—Dr Jackson

Psychotherapy is especially useful in elderly patients to avoid the adverse effects associated with medications.⁹

Sleep hygiene education should be included in Mrs J's treatment to ensure that poor sleep habits are not a factor in her insomnia. Patients should be encouraged to keep their bedrooms at a comfortable temperature, avoid distractions like watching television or reading in bed, keep a consistent sleep schedule, and avoid caffeinated drinks within several hours of bedtime (Figure 2).¹⁰

Figure 2. Dos and Don'ts of Sleep Hygiene^a



^aBased on American Sleep Association.¹⁰

Other external factors could also be contributing to Mrs J's depression and decreased social activity, such as loss of friends or family members, limited funds, or loss of functional independence because of problems with hearing or eyesight.¹¹ Addressing these concerns could help Mrs J regain her social activity and improve her depressive symptoms. Depression is not a normal or acceptable part of aging; no matter the patient's age, the goal of treatment should always be restoring patients to 100% mental wellness.

CONCLUSION

Patients like Mrs J have unrecognized residual symptoms related to depression that hinder their functioning and interaction with others. Using 3 approaches to identify symptoms, clinicians can get a clearer picture of what is troubling their patients. First, patients must

be questioned specifically about symptoms. Second, rating scales should be administered regularly to track symptoms and treatment response, and, third, collateral information should be gathered from patients' family members or friends. Clinicians should safely optimize the current medication dose and check antidepressant adherence as well as whether additional medications are interfering with response or causing symptoms. Augmenting or switching among pharmacologic and nonpharmacologic options may be necessary to alleviate symptoms and restore patients to full functioning.

Clinical Points

- ▶ Question patients and informants carefully regarding symptoms, related conditions, medications, and adherence when depression has not fully resolved
- ▶ Use rating scale results for additional information on symptoms and response
- ▶ Consider nonpharmacologic strategies such as psychotherapy and sleep hygiene education as well as pharmacologic strategies like switching or augmenting medications to help resolve residual depressive symptoms
- ▶ Individualize strategies based on safety for elderly patients

Drug names: alprazolam (Xanax and others), aripiprazole (Abilify and others), bupropion (Wellbutrin, Aplenzin, and others), lithium (Lithobid and others), quetiapine (Seroquel and others)

REFERENCES

1. Gislason T, Benediktsdóttir B, Björnsson JK, et al. Snoring, hypertension, and the sleep apnea syndrome. An epidemiologic survey of middle-aged women. *Chest*. 1993;103(4):1147–1151.
2. Johns MW. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. *Sleep*. 1991;14(6):540–545.
3. Furukawa TA, Streiner DL, Young LT. Antidepressant and benzodiazepine for major depression. *Cochrane Database Syst Rev*. 2002;1(1):CD001026.
4. American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2012;60(4):616–631.
5. Preston TC, Shelton RC. Treatment resistant depression: strategies for primary care. *Curr Psychiatry Rep*. 2013;15(7):370.
6. Dolder C, Nelson M, Stump A. Pharmacological and clinical profile of newer antidepressants: implications for the treatment of elderly patients. *Drugs Aging*. 2010;27(8):625–640.
7. Beers MH, Passman LJ. Antihypertensive medications and depression. *Drugs*. 1990;40(6):792–799.
8. Gareri P, Segura-García C, Manfredi VG, et al. Use of atypical antipsychotics in the elderly: a clinical review. *Clin Interv Aging*. 2014;9:1363–1373.
9. Moret C. Combination/augmentation strategies for improving the treatment of depression. *Neuropsychiatr Dis Treat*. 2005;1(4):301–309.
10. American Sleep Association. Sleep Hygiene Tips. <https://www.sleepassociation.org/patients-general-public/insomnia/sleep-hygiene-tips>. Reviewed September 2007. Accessed October 20, 2015.
11. American Psychological Association. Aging and Depression. <http://www.apa.org/helpcenter/aging-depression.aspx>. Accessed October 20, 2015.



POSTTEST

To obtain credit, go to PSYCHIATRIST.COM
(Keyword: Outcomes) to take this Posttest and complete the Evaluation.

1. Ms A, your 25-year-old patient with MDD, has responded well to SSRI treatment over 6 weeks, and her current PHQ-9 score is 6. However, she says she has continued feeling tense and worried nearly all the time. What would be the *preferred* next step in her assessment?
 - a. Administer the GAD-7 to screen for an anxiety disorder comorbidity
 - b. Administer the MDQ to see if she has unrecognized manic/hypomanic symptoms
 - c. Administer the ASRS to see if she has ADHD
 - d. Continue treatment without further assessment since her PHQ-9 score indicates only mild depression
2. Mr B, your 64-year-old patient with recurrent depression, presents with continued depression, irritability, and apathy. He has failed previous trials with sertraline and citalopram, and he is currently taking bupropion SR at a dose of 150 mg per day. Over the past 4 weeks his PHQ-9 score has decreased from 18 to 14. He is tolerating the medication well. What would be the current *preferred* treatment strategy for Mr B?
 - a. Augment bupropion with an atypical antipsychotic
 - b. Switch to an SNRI
 - c. Continue the current dose of bupropion to see if his mood improves with more time
 - d. Increase the dose of bupropion SR to 300 mg per day and have him return in 2 weeks for a reassessment

▶ CME BACKGROUND

To obtain credit, read the article, correctly answer the questions in the Posttest, and complete the Evaluation.

▶ CME OBJECTIVE

After studying this educational activity, you should be able to:

- Regularly assess patients with depression with validated instruments to monitor response to medication and residual symptoms

▶ ACCREDITATION STATEMENT

The CME Institute of Physicians Postgraduate Press, Inc., is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

▶ CREDIT DESIGNATION

The CME Institute of Physicians Postgraduate Press, Inc., designates this enduring material for a maximum of 1 *AMA PRA Category 1 Credit™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

The American Academy of Physician Assistants (AAPA) accepts certificates of participation for educational activities certified for *AMA PRA Category 1 Credit™* from organizations accredited by ACCME or a recognized state medical society. Physician assistants may receive a maximum of 1 hour of Category I credit for completing this program.

▶ DATE OF ORIGINAL RELEASE/REVIEW

This educational activity was published in December 2015 and is eligible for *AMA PRA Category 1 Credit™* through December 31, 2017. The latest review of this material was October 2015.

▶ STATEMENT OF NEED AND PURPOSE

Most patients are treated for depression by their primary care physician (PCP). Unfortunately, PCPs are less likely to provide guideline-concordant, measurement-based care than specialists. Optimal care for major depressive disorder (MDD) should involve regular assessment of symptom resolution, treatment adherence, and tolerability. PCPs need education about how to implement measurement-based care and

why it will save them time, as well as about how to encourage adherence and manage residual symptoms such as cognitive dysfunction. This activity was designed to meet the needs of participants in CME activities provided by the CME Institute of Physicians Postgraduate Press, Inc., who have requested information on the management of depression.

▶ DISCLOSURE OF OFF-LABEL USAGE

Dr Jain has determined that, to the best of his knowledge, bupropion and lithium are not approved by the US Food and Drug Administration for augmentation treatment of major depression.

▶ REVIEW PROCESS

The entire faculty of the series discussed the content at a peer-reviewed planning session, the Chair reviewed the activity for accuracy and fair balance, and a member of the External Advisory CME Board who is without conflict of interest reviewed the activity to determine whether the material is evidence-based and objective.



Board of Editors:
Editor in Chief Larry Culpepper, MD, MPH,
and Deputy Editor Pierre N. Tariot, MD

© Copyright 2015 Physicians Postgraduate Press, Inc.,
PO Box 752870, Memphis, TN 38175-2870;
PRIMARYCARECOMPANION.COM. All right reserved.

To listen to podcast discussions of the patient cases among faculty experts, go to **PSYCHIATRIST.COM**
Enter Keyword **DEPRESSION**

