Clinical Vignettes

By David Price, MD, FAAFP

Evidence-Based Clinical Vignettes from the Care Management Institute: Major Depression

Introduction

Depressive syndromes are commonly seen in the primary care setting. Major depression affects 4.8% to 8.6% of the general US population in any given year; other types of depression affect an additional 3% to 8.4% of patients.[1] Total costs of depression, including direct medical costs and indirect costs due to days lost from work, exceed $43 billion annually.[1,2]

In the primary care setting, treatment of depression usually includes evaluation by a physician, brief patient education, and either antidepressant therapy, referral to a behavioral health specialist, or both a prescription and a referral. Although most depressed patients can be successfully treated by primary care clinicians, depression remains unrecognized or undertreated in many patients.

In 2001, the Kaiser Permanente Care Management Institute (CMI) revised its guideline for evidence-based care of depressed adult outpatients in the primary care setting.[3] This article and case example highlight key steps and recommendations from this guideline.

Case Example

A 28-year-old married, employed female computer programmer with two young children (one aged four years, the other aged nine months) is seen for a four-week history of fatigue, insomnia, headache, abdominal discomfort, and difficulty concentrating at work. She denies signs and symptoms of an acute infectious process and did not have headache or abdominal pain before the previous month. She is breastfeeding. She has obtained intermittent relief from headache by using acetaminophen, and she takes a multivitamin regularly. Normal menses has resumed. She is appropriately and professionally dressed, and her children accompany her in the examination room. She appears tired but in no acute distress. Results of physical examination, including neurologic screening, are normal.

Table 1. Instruments reviewed by the CMI Depression Guideline Group to screen for major depressive disorder (MDD) in adults

Two-question screening:[14] • "During the past month, have you often been bothered by feeling down, depressed, or hopeless?" • "During the past month, have you often been bothered by little interest or pleasure in doing things?"
Beck Depression Inventory (BDI)[15]
Center for Epidemiologic Studies in Depression Scale (CES-D)[16]
Depression Arkansas Scale (D-ARK)[17]
Geriatric Depression Scale (GDS)[18]
Outcomes Questionnaire 45 (OQ-45)[19]
Primary Care Evaluation of Mental Disorders (Prime-MD)[20]
Patient Health Questionnaire (PHQ-9)[21]
Quick Diagnostics Panel (QPD)[22]
Zung Self-Rating Depression Scale (SDS)[23]

How should you proceed toward making a diagnosis? What treatment options are available? How should you follow this patient over time?

Definition of Major Depressive Disorder

Major depressive disorder (MDD) is characterized by at least two weeks of *either* depressed mood or loss of interest in previously pleasurable activities[4] along with four or more additional symptoms, including:

- guilt
- sleep disturbance
- psychomotor retardation or agitation
- appetite disturbance
- difficulty concentrating
- decreased energy
- suicidal ideation, intention, or plan[4]

The mnemonic device DIGSPACES is a helpful way to remember these key symptoms of MDD. Diagnosis and treatment of other types of depression (eg, adjustment disorder with depressed mood; dysthymia; minor depressive disorders; depression with psychotic features; and bipolar disorder) are beyond the scope of this article.

Who Should be Screened for Depression?

Patients with cancer,[5] chronic pain,[6] heart failure,[7] diabetes,[8] recent stroke,[9] or a recent acute cardiac event[10] have higher rates of depression than the general population. Elderly patients with multiple medical comorbidity may also be at increased risk for depression.[11] Patients with a prior history of MDD are at risk for recurrence.[2,12] Other patients—those

DAVID PRICE, MD, FAAFP, is Director of Education and a Clinical Researcher with the Colorado Permanente Medical Group. He is also Associate Professor of Family Medicine at the University of Colorado Health Science Center, Denver, CO. E-mail: david.price@kp.org.

with multiple somatic complaints without known cause, women in the antenatal and postpartum periods, victims of domestic abuse, and HIV-positive patients—may also be candidates for screening.

Some evidence indicates that one-time screening of adults 40 years of age or older may be cost-effective from a societal perspective.[1,13] However, screening of asymptomatic adults at low risk may result in many false-positive tests. Thus, clinicians should weigh the potential societal benefits of screening asymptomatic low-risk adults against other clinical and operational priorities (including depression screening of higher-risk patients).

Table 2. Selected differential diagnosis of MDD

Concurrent psychiatric conditions	Concurrent medical conditions	Medication-related
Adjustment disorder	Endocrine:	Antihypertensive/
Bipolar disorder	hypothyroidism	cardiovascular agents:
Dysthymia	Cushing's disease	reserpine
Personality disorder	Central nervous system:	clonidine
Psychotic depression	Parkinson's disease	methyldopa
Posttraumatic stress disorder/abuse	Alzheimer's disease	digitalis
Seasonal affective disorder	multiple sclerosis	hydralazine
Somatization	brain tumors	prazosin
Substance abuse	Cardiovascular system:	procainamide
	stroke	Sedative hypnotic agents:
	myocardial infarction	barbiturates
	congestive heart failure	chloral hydrate
	Miscellaneous:	benzodiazepines
	rheumatoid arthritis	Anti-inflammatory agents:
	AIDS	indomethacin
	pernicious anemia	pentazocine
	carcinoma	opiates
		Steroids:
		corticosteroids
		Interferon

Diagnosis of MDD

Several screening tools are available to assist clinicians in screening for depression (Table 1).[14-23] Many of these tools can be completed by the patient and easily scored by the clinician or by an assistant. These tools have similar false-positive and false-negative rates.[20,22,24-32] A "yes" answer to one of the following two questions is as sensitive a screen for MDD as most of these screening tools.[14]

- "During the past month, have you often been bothered by feeling down, depressed, or hopeless?"
- "During the past month, have you often been bothered by little interest or pleasure in doing things?"

All positive screening results should be confirmed with careful attention to possible substance abuse, medical, and other psychological causes or comorbidity (Table 2). The patient in the above example denied using alcohol or drugs and denied current or past physical, sexual, or emotional abuse; in addition, the complete blood cell count (CBC) and thyroid-stimulating hormone (TSH) level were normal. (TSH is measured to rule out hypothyroidism, a common postpartum condition that can cause depression.)

Assessing Severity of Depressive Symptoms

Symptom severity is an important guide to selecting proper treatment for MDD. Many depression-screening instruments provide a range of scores corresponding to mild, moderate, and severe depression. Patients with five or six symptoms of MDD who have slightly impaired daily functioning are mildly depressed. Patients with six or seven MDD symptoms and moderately impaired daily functioning are moderately depressed. Patients with eight or nine MDD symptoms with profoundly impaired functioning in daily activities or suicidal intention or plans are severely depressed.

Assessing Suicidal Ideation

All depressed patients, regardless of illness severity, should be screened for suicidal ideation. Many patients with depression have thoughts of suicide; asking "Have you thought about taking your life?" does not make patients more prone to attempt suicide. Patients with current suicidal ideation should be asked about their intentions ("Do you think you will commit suicide?") and if they have a plan ("Have you thought about how you would kill yourself?" "Do you plan to kill yourself? If so, when?"). Clinicians should elicit a promise from actively suicidal patients not to harm themselves and should assess adequacy and availability of patient support systems

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(family, friends, and clergy). A behavioral health specialist should be contacted immediately in these cases. Risk factors for suicide include: recent loss; medical hospitalization within the past year; history of psychiatric hospitalization or suicide attempts; living alone; severe vegetative symptoms; severe hopelessness; comorbid substance abuse; and other comorbid psychiatric conditions. Patients with these risk factors should be closely monitored.[33-36] Although men are statistically more likely than women to successfully commit suicide, women attempt suicide more often.[37]

Treatment of MDD

Medication vs Psychotherapy

For most mildly or moderately depressed adult primary care outpatients, medication and psychotherapy are equally effective,[38-41] although psychotherapy might be slower to take effect.[40,41] A shared decision-making approach describing the pros and cons of each option should be used with these patients to help them select initial treatment options consistent with their values and concerns. One study[41] found that patients who select psychotherapy achieve better outcomes than patients who are "assigned" to it. Another study[42] found that patients of different cultural backgrounds often prefer psychotherapy to medication. A shared decision-making approach in patients with other conditions has been shown to improve patient knowledge and to decrease patient uncertainty about type of treatment.[43-45] This approach can also help instill a sense of control in depressed patients, who often feel "lost" as a result of their depression.

Severely depressed patients may respond better to medication than psychotherapy[46] and may respond better to the combination of medication and psychotherapy.[46,47] Consultation with a psychiatrist or other behavioral health specialist is recommended for severely depressed patients seen in the primary care setting.

Types of Antidepressant Medication

All antidepressant classes appear to be equally effective in depressed patients regardless of their age[48] and regardless of whether they are affected by any of the following conditions: diabetes;[49,50] cancer;[51,52] recurrent, chronic, or refractory depression;[53-59] or mixed anxiety and depression.[59-65] The CMI Depression Guideline group did not find high-quality studies comparing the effectiveness of different antidepressants in patients of different ethnic groups.

In the first six to 12 weeks of therapy, selective serotonin reuptake inhibitors (SSRIs) are somewhat better tolerated than tricyclic agents (TCAs) (number needed to treat, 20-33).[66,67] Risk of death by overdose is greater with TCAs than with SSRIs, although rate of suicide from all causes does not differ on the basis of type of antidepressant.[59,68,69] However, given the lethality of TCAs when overdosed, the CMI guideline workgroup strongly recommends that TCAs be avoided by patients who are suicidal. Antidepressant agents have different side effect profiles that clinicians should consider when prescribing for patients with other comorbidities; patients may express a preference for a type of medication on the basis of discussing class-specific side effects with the clinician.

Patients successfully treated for depression with a particular antidepressant in the past should be offered that agent again. Partly on the basis of favorable pricing obtained from the manufacturer, fluoxetine is now Kaiser Permanente's preferred SSRI.

Hypericum (St John's wort) has been shown to be as effective as low-dose TCAs or SSRIs in treatment of mildly depressed adults and is better tolerated than TCAs.[59,70-75] However, the CMI depression guideline workgroup has several concerns regarding the trials studying St John's wort, including difficulty in blinding as well as lack of standardized preparations across trials. The US Food and Drug Administration (FDA) does not regulate St John's wort, and the amount of active ingredient may vary widely between and within brands. For these reasons, the CMI guideline workgroup recommends caution in prescribing St John's wort for treatment of depression. Clinicians should consider discussing these concerns with patients who wish to use St John's wort. This substance should not be used in combination with other antidepressant agents.

Treatment Phases and Follow-up

Acute Phase

The acute phase of treatment for MDD is defined as the period extending from the start of treatment that achieves symptom remission for a period of three months. No scientific evidence suggests an optimal frequency of follow-up during the acute phase, but Health Plan Employer Data Information Set (HEDIS) criteria require three follow-up contacts (including one face-to-face contact with a prescribing provider) in the first 12 weeks of treatment.[76] The risk of patients discontinuing treatment is

highest in the first months of treatment;[67] therefore, follow-up is needed to assess patient adherence to therapy, symptom remission, and, if medication is chosen, presence of worrisome or unacceptable side effects.

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Several options are available for patients who do not achieve symptom remission within 6 to 12 weeks. The diagnosis should be reevaluated, and possible presence of other untreated comorbid conditions should be considered. Adherence to treatment regimen should be assessed and reinforced. Dosage of medication may be increased or the medication can be changed. Psychotherapy and medication can be combined, or a second, low-dose antidepressant from a different class can be added. At this point, referral to a behavioral health specialist is also an available option for patients who do not respond to prescribed medication.

Continuation Phase

After the acute phase has ended, patients should continue treatment for an additional 4 to 12 months. Terminating treatment sooner is associated with early recurrence of symptoms.[77] No available data exist to suggest an optimal frequency of patient follow-up during the continuation phase. The CMI guideline panel consensus opinion recommends at least one follow-up during the fifth or sixth month of treatment to assure continued remission of symptoms and patient adherence to treatment as well as to determine necessity of adjusting treatment. More frequent follow-up can be scheduled on the basis of clinical judgment and patient preference.

Discontinuation

After successfully completing treatment in the acute and continuation phases, patients for whom the treated episode was the first should be offered a trial of medication discontinuation.[12] Fluoxetine regimens of less than 20 mg daily can be stopped; higher fluoxetine doses and other medications should be tapered over a two- to four-week period.[78,79] Because a single episode of MDD is associated with a 50% lifetime risk of recurrence,[2] patients with MDD should be educated about this risk and instructed to call their clinician at the first signs or symptoms of recurrent MDD. Data suggest that risk of recurrence is highest during the first year after medication is discontinued.[12] The CMI guideline panel suggests that patients be reassessed three months after discontinuing medication and again at 12 months.

Maintenance

Patients who have had three or more episodes of MDD have a 90% lifetime risk of recurrence after medication discontinuation.[2] Studies[12,80] suggest that continuing medication for at least five years is beneficial for these patients because it decreases risk of relapse. No available data exist to suggest an optimal frequency of patient follow-up during maintenance treatment. The CMI guideline recommends at least one annual contact with the patient to detect symptom relapse and to determine need for treatment adjustment.

Table 3. Script for explaining the diagnosis of depression to patients

"Depression isn't all in your head, and it's not a personal failing. It's a real illness caused by imbalance of chemicals in your body—just like diabetes. In diabetes, your body chemicals get out of balance and can't control your blood sugar. In depression, chemicals in your brain get out of balance, and it affects the way you think, act, and feel."

Table 4. Patient instructions for taking medication

It's important to take your medication every day as prescribed.
Antidepressants must be taken for two to six weeks to see a noticeable effect on depressive symptoms.
It's important to take your medication even after you feel better or else your depression can quickly come back.
Antidepressant medication must be taken for a *minimum* of 7-12 months.
Most side effects are temporary and resolve within a few weeks. (Give specifics on how to manage specific side effects). Call if you have any side effects that concern you or you cannot tolerate.
Do not stop taking this medication without checking with your primary care doctor or a prescribing clinician.

Adapted by permission of the publisher (http://lww.com) and author from: Lin EW, 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.[82]

No evidence is available to indicate the best therapeutic approach (maintenance vs discontinuation) for patients who have had two episodes of MDD. Expert opinion[81] suggests that if these patients have a history of suicide attempt, substance abuse, or psychiatric comorbidity, they should continue maintenance therapy. For patients experiencing their second episode of MDD without these types of comorbidity, a shared decision-making approach should be used for selecting maintenance or discontinuation of treatment. For these patients, the lifetime risk of MDD recurrence is approximately 70%;[2] therefore, these patients should receive both follow-up and patient education on symptom relapse.

Patient Education

Despite a trend toward increasing acceptance, many patients still feel stigmatized by the diagnosis of MDD. Therefore, clinicians should explain to these patients that MDD is a real illness and is not "all in their head." Comparison with diabetes may be helpful (Table 3). Patients choosing medication should be informed about side effects and given instructions designed to enhance compliance with prescribed medication regimens (Table 4).[82] Patients should also be educated about the signs and symptoms of relapsing or worsening depression.

Table 5. Consensus criteria for referral to a behavioral health specialist

Two months of treatment without desired clinical improvement
Active homicidal ideation
Active suicidal ideation
Bipolar or manic behavior
Counseling with or without medication
Difficulty adhering to treatment plans
Domestic violence
Failure to respond to second antidepressant
Lifelong/recurrent depressions
Partial response to medication
Psychotic symptoms
Significant alcohol/other substance abuse
Unclear diagnosis

Specialty Referral

The CMI Depression Guideline workgroup recommends referral or consultation with a behavioral health specialist for the situations listed in Table 5.[3]

Case Example—Diagnostic and Treatment Approach

In addition to sleep disturbance, decreased energy, and difficulty concentrating, the patient in the above example admitted being sad and tearful as well as feeling guilty and worrying about her parenting skills, and she had lost interest in socializing. She also admitted to worrying about work performance and being somewhat irritable with her husband. She was not suicidal and had no prior history of depression or other psychiatric illness, but she thought her mother may have been depressed. Other medical comorbidity was excluded, and she was diagnosed with MDD, first episode, with secondary anxiety (not meeting criteria for generalized anxiety disorder). After participating in a shared decision-making approach, she selected pharmacotherapy with a SSRI and started fluoxetine, 10 mg daily, the next morning. At two-week follow-up, her depressed mood and energy were "50% better," but she was still having trouble concentrating and sleeping and was still irritable. The dose of fluoxetine was increased to 20 mg in the morning, and 50 mg of trazodone was added at bedtime. At six-week follow-up, she was sleeping better, and her depressed mood and guilt about parenting were "almost gone." Her energy was "returning to normal," but she still worried about her work performance and reported having continued irritability with her husband. She elected not to change her medication regimen or to add psychotherapy and, at 12-week follow-up, reported total symptom resolution.

She remained on medication, without further symptoms, for one year (three months of acute-phase treatment plus nine months of continuation-phase treatment). She was then offered—and elected—a trial of medication discontinuation. Follow-up calls at three weeks and at three months revealed continued absence of symptoms. During a health maintenance visit one year after medication discontinuation, she reported slight decrease in appetite as well as increase in worry and irritability, which she attributed to job stress. Repeat screening was not diagnostic for recurrent MDD or anxiety. The patient was reeducated on the symptoms of MDD and elected to monitor symptoms without resuming medication. At follow-up three months, six months, and 12 months later, the symptoms had resolved, and the patient remained in remission.

Conclusion

CMI recently completed an extensive, evidence-based revision of the adult depression guideline,[3] which also discusses different cultural backgrounds, the elderly, and (briefly) depression among adolescents. The guideline group views the depression guideline as a work in progress: Future revisions will update current evidence and explore evidence in areas not cov-

ered in the current guideline. The full document will be available on the Permanente Knowledge Connection Web site: http://pkc.kp.org/national/cmi/programs/depression/DP_Guidelines.html. ❖

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Practice Tips

Screen patients for depression who have: • a history of past depression • cancer
Consider screening for depression patients who have any of the following medical comorbidity: • congestive heart failure • patients in the first three to six months after myocardial infarction, coronary artery bypass surgery, or angioplasty • patients three to six months after a cerebrovascular accident • chronic pain • patients over age 60 years, especially those with multiple medical comorbidity and when psychosocial conditions change
A number of depression screening instruments may be considered. Asking two questions (four-week duration of depressed mood or loss of interest in previously pleasurable activities) is a time-efficient and accurate method of screening. • Positive depression screening should be further investigated to appropriately diagnose and classify patients to determine appropriate treatment strategies.
All depressed patients should be assessed for suicidal ideation, intention, and plan.
Antidepressants and psychotherapy are equally effective for most mildly to moderately depressed patients seen in the primary care setting.
All classes of antidepressants are equally effective in treating depression.
Selective serotonin reuptake inhibitors (SSRIs) have a slight short-term advantage over tricyclic antidepressants (TCAs) in short term (6-12 weeks) adherence rates (number needed to treat = 20 to 33). Caution should be used in extrapolating these data to longer-term medication adherence rates.
Hypericum (St John's wort) should not be used for severely depressed patients.
Antidepressant medication should be continued through the acute phase (three months of treatment that achieves symptom resolution) *plus* an additional 4-12 months.
Patients with a history of one lifetime episode of MDD are candidates for a trial of medication discontinuation after symptom resolution following adequate acute and continuation phase.
Patients with a history of three or more episodes of MDD should be maintained on medication for a period of at least five years.

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Time

By losing present time, we lose all time.

W Gurney Benham, 1859–1944, Mayor of Colchester, England, 1892