in the clinic

Depression

Section Editors
David Goldmann, MD
Christine Laine, MD, MPH

Physician Writers
Tonya Fancher, MD
Richard Kravitz, MD

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Depression is common in primary care, affecting 5% to 10% of patients in this setting (1). Untreated depression may be a barrier to effective treatment of common co-occurring illnesses (e.g., diabetes and cardiovascular disease) (2). The disability associated with depression is similar to that of other chronic medical conditions (3). Depression is currently the fourth leading contributor to the global burden of disease (as measured using disability-adjusted life-years) and will move into second place by 2020 (4). Effective treatment of depression reduces symptoms and improves quality of life (5). Although sometimes viewed as "opening Pandora's box," primary care clinicians can efficiently identify and manage most cases of depression.

Screening

Which patients are at especially high risk for depression?

Screening limited to high-risk adults (i.e., case-finding) may be more cost-effective than screening all adults. Risk factors for depression include older age (6) and associated neurologic conditions, recent childbirth (7), stressful life events (8), a personal or family history of depression, and selected medical comorbid conditions (9) (Table 1). Suicide rates are twice as high in families of suicide victims (10).

Should clinicians screen for depression?

A 2002 U.S. Preventive Services Task Force reviewed 14 randomized, controlled trials examining the effectiveness of screening for depression in primary care. This guideline recommends screening adults for depression in clinical practices that have "systems in place to assure accurate diagnosis, effective treatment, and follow-up" (1). Depression screening instruments do not diagnose depression but do accurately identify patients at risk. All positive screening tests should trigger a full diagnostic interview to determine the presence or absence of specific depressive disorders.

A meta-analysis of screening studies suggested that screening is associated with a 9% absolute reduction in the proportion of patients with persistent depression at 6 months. Assuming a prevalence of 10%, 110 primary care patients would need to be screened for depression to produce 1 additional remission (1).

How often should clinicians screen for depression?

The optimal interval for screening is unknown. Based on expert recommendations, clinicians should consider screening patients with identified risk factors (Table 1) and those with several unexplained or unrelated somatic symptoms, comorbid psychological conditions (e.g., panic disorder or generalized anxiety), substance abuse, chronic pain, or lack of response to usually effective treatments for comorbid medical conditions (11).

What methods should clinicians use to screen for depression?

A positive response to a 2-item instrument (see the Box on the next page) had a sensitivity of 96% and a specificity of 57%.

Table 1. Risk Factors for Depression

Risk Factor	
Older age (including associated neurologic conditions, such as Alzheimer disease and parkinsonism)	Prevalence 7% to 36% for persons over age 65 years; 40% for those with Alzheimer disease; 50% for those with Parkinson disease
Recent childbirth	13%
Recent stressful events	Variable
Personal or family history of depression	30% of patients experience recurrence within 2 years of initial diagnosis and 87% within 15 years
Comorbid conditions	2-fold increase in risk for depression among patients with diabetes, coronary artery disease, stroke, obesity, and HIV infection

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3. Hays RD, Wells KB, Sherbourne CD, Rogers W, Spritzer K. Functioning and well-being outcomes of patients with depression compared with chronic general medical illnesses. Arch Gen Psychiatry. 1995;52:11-9. [PMID: 7811158]
4. Remick RA. Diagnosis and management of depression in primary care: a clinical update and review. CMAJ. 2002;167:1253-60. [PMID: 12451082]
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6. McDonald WM, Richard IH, DeLong MR. Prevalence, etiology, and treatment of depression in Parkinson's disease. Biol Psychiatry. 2003;54:363-75. [PMID: 12893111]
7. Beck CT. Predictors of postpartum depression: an update. Nurs Res. 2001;50:275-85. [PMID: 11570712]

Table 2. Screening Measures for Depression*

Screening Measure	*Items, n*	*Time Frame*	*Available in Spanish*	*Administration Time, min*
Primary Care Evaluation of Mental Disorders (PRIME-MD)	2	Past month	Yes	<2
Beck Depression Inventory (BDI)	21	Today	Yes	5–10
Center for Epidemiological Studies Depression Scale (CES-D)	20	Past week	Yes	5–10
General Health Questionnaire (GHQ)	28	Past few weeks	N/A	5–10
Medical Outcomes Study Depression Screen (MOS-D)	8	Past week	N/A	<2
Symptom-Driven Diagnostic System Primary Care (SDDS-PC)	5	Past month	N/A	<2
Zung Self-Depression Scale (SDS)	20	Recently	No	5–10
Hopkins Symptom Checklist-25	25	Past week	Yes and others	5–10
Geriatric Depression Scale (GDS)†	30	Past week	Yes	10–15
Cornell Scale for Depression in Dementia†	19	Past week	No	10–15
Hamilton Rating Scale for Depression†	21	N/A	No	10–15
Edinburgh Postnatal Depression Scale‡	10	Past week	Yes	5–10

** Adapted from Mulrow CD, Williams, JW Jr, Gerety MB, et al. Case-finding instruments for depression in primary care settings. Ann Intern Med. 1995;122:913-21. Sharp LK, Lipsky MS. Screening for depression across the lifespan: a review of measures for use in primary care settings. Am Fam Physician. 2002;66:1001-8.*

† For use in elderly patients (>65 years of age). ‡ For use in postpartum women.

Patients with a positive response to 1 or both questions (i.e., those with depressed mood and/or anhedonia) should undergo a full diagnostic interview to assess whether they meet the criteria for depression disorders as set forth in the *Diagnostic and Statistical Manual of Mental Disorders, fourth edition* (DSM-IV) (see Table 3 in Diagnosis).

A meta-analysis of 9 case-finding instruments in 18 studies and a head-to-head study of screening instruments showed that the 2-question instrument is as good as many of the longer instruments (12).

Many other screening tools, targeted to specific populations, are available (Table 2). The most commonly used screening tools in adults include the Beck Depression Inventory Scales II, the Center for Epidemiologic Studies Depression Scale-Revised, and the Zung Self-Rating Depression Scale. The Edinburgh Postnatal Depression Scale was specifically developed to assess postpartum depression (12–14). In the elderly, cognitive impairment can limit the utility of screening instruments and should be assessed with the Mini-Mental State Examination. In patients with cognitive deficits, clinicians should consider the interviewer-administered Cornell Scale for Depression in Dementia or the Hamilton Rating Scale (15, 16). Several tools are available in non-English versions. The Hopkins Symptom Checklist-25 has been validated in refugee populations and is available in many languages.

Screening Questions for Depression

"Over the past 2 weeks have you felt down, depressed, hopeless?"

"Over the past 2 weeks have you felt little interest or pleasure in doing things?"

Screening... Clinicians should screen for depression as the first step in a systematic evaluation of mood disorders in all adults. Adults who are older, are postpartum, have a personal or family history of depression, or have comorbid medical illness are at increased risk. There is little evidence to recommend one screening method over another, so physicians can choose the method that best suits their patient population and practice setting. The 2-question instrument is more efficient and performs as well as longer instruments.

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12. Mulrow CD, Williams JW Jr., Gerety MB, et al. Case-finding instruments for depression in primary care settings. Ann Intern Med. 1995;122:913-21. [PMID: 7755226]
13. Beck AT, Steer RA, Brown GK. BDI-II, Beck Depression Inventory: Manual. 2nd ed. Boston: Harcourt Brace; 1996.

Diagnosis

What are the diagnostic criteria for depression?

Depression is diagnosed when 5 or more DSM-IV symptoms occur in the same 2-week period in conjunction with a change from previous functioning (Table 3) (17). At least one of the symptoms must be either depressed mood or anhedonia, as reflected in the 2-question depression screening model mentioned earlier.

An alternative strategy for diagnosing major depressive disorders is to follow the 2-item (mood and anhedonia) case-finding questions with assessment of the so-called SALSA inventory:

- Sleep disturbance
- Anhedonia
- Low Self-esteem
- Appetite disturbance

Patients with 2 of these 4 symptoms occurring nearly every day for at least 2 weeks are virtually identical to those diagnosed using the 5-out-of-9-symptom algorithm in Table 3. Over 97% of patients with major depression have at least 2 of the SALSA symptoms. Only 6% of persons who do not have major depression will have 2 of the SALSA symptoms (18).

How can clinicians determine the severity of depression?

Assessment of depressive symptom severity helps guide treatment. Mild to moderate depression responds equally well to either medication or psychotherapy (19). Patients with severe major depressive disorder benefit more from antidepressant medication or from medication combined with psychotherapy than from psychotherapy alone.

The self-administered 9-item Patient Health Questionnaire (PHQ-9) is easily scored to quantify the severity of depression (Table 4) (20). Items 1 through 9 are summed to yield a scale score ranging from 0 to 27. On this scale, 0 to 4 is considered nondepressed, 5 to 9 mild depression, 10 to 14 moderate depression, 15 to 19 moderately severe depression, and 20 to 27 severe depression. The 9 items reflect the 9 DSM-IV criteria. Item 10 assesses functional impairment. Like symptom severity, severe functional impairment may suggest the need for hospitalization and psychiatric consultation (21).

How can clinicians and patients distinguish between normal reactions to life events and depression?

Situational adjustment reaction with depressed mood is subsyndromal depression with a clear precipitant. Subsyndromal (minor) depression is characterized by 2 to 4 DSM-IV depressive symptoms, including depressed mood or anhedonia, for more than 2 weeks (Table 3). Adjustment disorder usually abates with resolution of the stressor, but careful observation and supportive counseling are indicated.

Differentiating normal grieving and pathologic grief from depression can be difficult. The syndrome of major depression may be transiently present in normal grief; however, sadness without the complete syndrome is more common. Transient hallucinations (hearing or seeing the deceased person) or suicidal thoughts (feeling that one would be better off dead or should have died with the deceased person) are considered a normal part of grief. The boundaries of normal grief are affected by cultural and societal factors. Symptoms suggestive of depression include inappropriate guilt, persistent thoughts of death, morbid preoccupation with worthlessness, marked psychomotor retardation, prolonged functional impairment, and hallucinations. Patients whose symptoms persist beyond 2 months should be evaluated for depression.

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15. Alexopoulos GS, Abrams RC, Young RC, Shamoian CA. Cornell Scale for Depression in Dementia. Biol Psychiatry. 1988;23:271-84. [PMID: 3337862]
16. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry. 1960;23:56-62. [PMID: 14399272]
17. Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). 4th ed. Washington, DC: American Psychiatric Association; 1994.
18. Brody DS, Hahn SR, Spitzer RL, et al. Identifying patients with depression in the primary care setting: a more efficient method. Arch Intern Med. 1998;158:2469-75. [PMID: 9855385]

Table 3. Criteria for Major Depressive Episode on the Basis of the *Diagnostic and Statistical Manual of Mental Disorders

Five or more of the following symptoms (one of which is depressed mood or loss of interest or pleasure) have occurred together for a 2-week period and represent a change from previous functioning:

- Depressed mood most of the day, nearly every day as self-reported or observed by others
- Diminished interest or pleasure in all or almost all activities most of the day, nearly every day
- Significant weight loss when not dieting, or weight gain; or decrease or increase in appetite nearly every day
- Insomnia or hypersomnia nearly every day
- Psychomotor agitation or retardation nearly every day
- Fatigue or loss of energy nearly every day
- Feelings of worthlessness or excessive or inappropriate guilt nearly every day
- Diminished ability to think or concentrate nearly every day
- Recurrent thoughts of death, recurrent suicidal ideation without a specific plan.

The symptoms do not meet criteria for a mixed episode.

The symptoms cause clinically significant distress or impairment in social, occupational, or other areas of functioning.

The symptoms are not due to the direct physiologic effects of a substance (drug or medication) or a general medical condition (hypothyroidism).

The symptoms are not better accounted for by bereavement, or the symptoms persist for more than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

** From American Psychiatric Association. Guidelines for the Treatment of Patients with Major Depressive Disorder. Washington, DC: American Psychiatric Publishing, Inc.; 1994. Reproduced with permission.*

What alternative medical or psychiatric disorders should clinicians consider when evaluating patients with symptoms of depression?

Certain medications and comorbid conditions are known to be associated with clinical depression. Glucocorticoids, interferon, l-dopa, propanolol, and oral contraceptives are the most commonly implicated medications. Data on isotretinoin remain unclear (22). The clinical situation will guide the clinician in choosing to discontinue the suspected agent or to add antidepressant therapy.

Depression can be a manifestation of hypothyroidism, Cushing disease, or cobalamin deficiency, and depression

Table 4. Patient Health Questionnaire-9*

Over the last 2 weeks, how often have you been bothered by any of the following problems? (0 = not at all; 1 = several days; 2 = more than one half the days; 3 = nearly every day)

1. Little interest or pleasure in doing things
2. Feeling down, depressed, or hopeless
3. Trouble falling or staying asleep or sleeping too much
4. Feeling tired or having little energy
5. Poor appetite or overeating
6. Feeling bad about yourself or that you are a failure or have let yourself or your family down
7. Trouble concentrating on things, such as reading the newspaper or watching television
8. Moving or speaking so slowly that other people have noticed or the opposite (i.e., being so fidgety or restless that you have been moving around a lot more than usual)
9. Thoughts that you would be better off dead or hurting yourself in some way
10. If you have checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

** The 9 items reflect the 9 DSM-IV criteria. Item 10 assesses functional impairment. Like symptom severity, severe functional impairment may suggest the need for hospitalization and psychiatric consultation. ©1999 Pfizer Inc. All rights reserved. Reproduced with permission.*

19. Thase ME, Greenhouse JB, Frank E, et al. Treatment of major depression with psychotherapy or psychotherapy-pharmacotherapy combinations. Arch Gen Psychiatry. 1997;54:1009-15. [PMID: 9366657]
20. Löwe B, Unützer J, Callahan CM, Perkins AJ, Kroenke K. Monitoring depression treatment outcomes with the patient health questionnaire-9. Med Care. 2004;42:1194-201. [PMID: 15550799]
21. Depression Guideline Panel. Depression in Primary Care: Treatment for Major Depression, Volume 2. Clinical Practice Guideline No. 5. Rockville, MD: US Department of Health and Human Services Agency for Health Care Policy and Research; 1993.

Clinicians should assess for suicidal ideation at each visit for depression.

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27. Depression Guideline Panel. Depression in Primary Care: Detection and Diagnosis, Volume 1. Clinical Practice Guideline No. 5. Rockville, MD: US Department of Health and Human Services Agency for Health Care Policy and Research; 1993.
28. Geringer ES, Perlmuter LC, Stern TA, Nathan DM. Depression and diabetic neuropathy: a complex relationship. J Geriatr Psychiatry Neurol. 1988;1:11-5. [PMID: 3252874]
29. Moscicki EK. Identification of suicide risk factors using epidemiologic studies. Psychiatr Clin North Am. 1997;20:499-517. [PMID: 9323310]

can co-occur with diabetes, stroke, and myocardial infarction (23-28). It can also be associated with somatization, anxiety, domestic violence, cognitive dysfunction, and alcohol dependence.

How should clinicians assess a depressed patient's risk for self–harm, including suicide?

Each year, more than 30,000 Americans commit suicide. Mental and addictive disorders, such as alcohol abuse, are the most powerful risk factors for suicide in all age groups, accounting for over 90% of all suicides (29). In evaluating a patient with major depression, previous suicide attempts should be considered the best predictor of completed suicide (30). Most patients who commit suicide have seen a physician in the preceding months. Clinicians should assess for suicidal intent at each visit for depression.

Asking about and reducing access to lethal means (especially firearms) can reduce the risk for suicide (31). A recent report also suggests that close telephone follow-up by an experienced psychiatrist can reduce the risk for suicide after a prior suicide attempt (32). Accurate assessment of suicidal risk and consideration of hospitalization is critical. Clinicians should consult a psychiatrist if there is any uncertainty regarding suicidal risk. In patients with suicidal ideation, the "No Harm Contract" (33) is a verbal or written agreement in which suicidal patients are asked to agree not to harm or kill themselves for a particular period.

In the absence of exacerbating factors, if the patient has good social support and is able to make a contract for safety, the clinician can proceed with outpatient treatment and close follow-up. If the patient has poor social support, cannot contract for safety, or is currently intoxicated, the clinician should choose emergency referral for hospitalization and psychiatric assessment.

When should clinicians consult a mental health professional for help diagnosing depression or a related mood disorder?

While many mood disorders can be successfully managed by the primary care clinician, psychiatric consultation should be considered when diagnostic uncertainty, significant psychiatric comorbidity, or significant suicidal ideation is present. Common diagnostic consultations involve patients with prolonged grieving, atypical symptoms with significant functional impairment, patients with a history suggestive of bipolar illness, or those on multiple medications. Cultural consultations to aid in the diagnosis and treatment for depression in culturally diverse populations are available in some settings (34).

The syndrome of major depression can be a presenting feature of other mental disorders. Clinicians should assess patients for psychotic disorders (delusions, hallucinations, disorganized speech, or episodes of catatonia) and substance abuse. Patients with psychotic symptoms or comorbid substance abuse are at greater risk for suicide and warrant psychiatric evaluation (35).

It is important to screen patients for a history of manic episodes (periods of days to weeks marked by unusually high energy, euphoria, hyperactivity, or impaired judgment). Patients with undiagnosed bipolar affective disorder who present with depressed mood may convert to frank mania if they receive antidepressant medication without a concurrent mood-stabilizing medication. If a patient develops manic or hypomanic symptoms after starting an antidepressant, consulting a psychiatrist is recommended. Delays in initiation of mood-stabilizing drug therapy at illness onset in bipolar disorder, even for relatively mild symptoms, may confer elevated risk for suicidal behavior, poorer social adjustment, and more hospitalizations (36).

Diagnosis... The DSM-IV criteria are the standard for diagnosing major depression. The risk for suicide and comorbid mental and physical illness should be assessed in each patient. If clinicians are uncertain about the diagnosis, risk for suicide, or need for hospitalization, psychiatric consultation should be considered.

CLINICAL BOTTOM LINE

Treatment

How should clinicians decide whether to recommend psychotherapy, drug therapy, or both?

Patients with mild to moderate major depression will benefit equally from psychotherapy or medication (19); combined therapy offers no demonstrated short-term benefit in these groups. Informed patient preference should influence choice of initial therapy. In some areas, therapist availability and insurance policies remain barriers to care. Clinicians should help patients to identify appropriate psychotherapy providers and willingly reevaluate initiating pharmacotherapy if access is difficult.

Severely depressed patients benefit more from antidepressant medication than psychotherapy alone. The greatest benefit could be derived from combined medication and psychotherapy.

A meta-analysis of original data from 595 patients with major depression comparing interpersonal therapy or cognitive therapy alone with interpersonal therapy plus antidepressants showed that combined therapy was superior to psychotherapy alone in severely depressed patients (19).

What types of behavioral interventions and psychotherapy are most likely to be effective for depression?

Some patients with mild depression may prefer an initial trial of a self-help book on cognitive behavioral techniques, such as *Feeling Good: The New Mood Therapy* by David D. Burns (37).

A meta-analysis of so-called "bibliotherapy" found a large improvement at 4 weeks; however, the participants appeared to have a very high educational level (38).

Behavioral interventions and psychotherapy require specialized training. Three types of psychotherapeutic options have proven effective: cognitive behavioral therapy, interpersonal therapy, and problem-solving therapy. Cognitive behavioral therapy aims to modify thoughts and behaviors to yield positive emotions. This therapy has also been used to treat residual symptoms after drug therapy and may help prevent relapse in patients with recurrent depression (39). Interpersonal therapy targets such interpersonal events as conflicts and role transitions that seem to contribute to the current depressive episode. This therapy is useful only if the patient has the capacity for psychological insight and is committed to longer-term therapy. Problem-solving therapy teaches patients how to improve their ability to deal with their specific everyday problems. Therapists often use a combination of the 3 therapies.

How should clinicians select from among the many antidepressant drug therapies?

Clinicians face a wide array of antidepressant drug options (Table 5). The most commonly prescribed antidepressants are classified as selective serotonin reuptake inhibitors (SSRIs). Other agents include monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs), serotonin norepinephrine reuptake inhibitors (SNRIs), 5-HT_2–receptor antagonists, and dopamine reuptake inhibitors.

Generally, MAOIs are used infrequently, even by psychiatric specialists, because of the long list of dietary

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32. Vaiva G, Vaiva G, Ducrocq F, et al. Effect of telephone contact on further suicide attempts in patients discharged from an emergency department: randomised controlled study. BMJ. 2006;332:1241-5. [PMID: 16735333]
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35. Hofmann DP, Dubovsky SL. Depression and suicide assessment. Emerg Med Clin North Am. 1991;9:107-21. [PMID: 2001661]
36. Goldberg JF, Ernst CL. Features associated with the delayed initiation of mood stabilizers at illness onset in bipolar disorder. J Clin Psychiatry. 2002;63:985-91. [PMID: 12444811]
37. Burns DD. Feeling Good-The New Mood Therapy Revised and Updated. New York: Avon; 1999.
38. Anderson L, Lewis G, Araya R, et al. Self-help books for depression: how can practitioners and patients make the right choice? Br J Gen Pract. 2005;55:387-92. [PMID: 15904559]

Table 5. Drug Treatment for Depression*

Agent, Daily Dosage	*Benefits*	*Side Effects*	*Notes*
SSRI			
Citalopram, 20–60 mg (10–40 mg) Escitalopram, 5–20 mg (5–10 mg) Fluoxetine, 20–60 mg (5–40 mg) Fluvoxamine, 100–300 mg Paroxetine, 20–50 mg (5–40 mg) Sertraline, 50–200 mg (2.5–150 mg)	Effective, well tolerated, lower risk for overdose compared with TCAs	Nausea, diarrhea, decreased appetite, anxiety, nervousness, insomnia, somnolence, sweating, impaired sexual function	All contraindicated with MAOIs; all have potential for drug interactions with hepatically metabolized drugs Fluvoxamine: nausea common Paroxetine: withdrawal syndrome not uncommon; FDA advisory that it should generally not be initiated in women who are in their first trimester of pregnancy or in those planning to become pregnant, but for some, the benefits of continuing paroxetine may outweigh the potential risk to the fetus
SNRI			
Venlafaxine, 75–350 mg (50–225 mg) Duloxetine, 30–60 mg Mirtazapine, 15–45 mg (7.5–30 mg)	Venlafaxine: effective, well tolerated, lower risk for overdose than TCAs Mirtazapine may be effective when other agents have not been	Venlafaxine: nausea, dry mouth, anorexia, constipation, dizziness, somnolence, insomnia, nervousness, sweating, abnormalities of sexual function; cardiovascular effects Mirtazapine: high incidences of somnolence, dizziness, weight gain, increased cholesterol, elevated liver transaminases, orthostatic hypotension; possible agranulocytosis	Venlafaxine: contraindicated with MAOIs; may cause sustained treatment-emergent hypertension, nervousness, and insomnia Mirtazapine: use caution with renal impairment; do not use with MAOIs; avoid diazepam and similar drugs
Norepinephrine uptake inhibitor			
Maprotiline, 25–225 mg	Fewer side effects than TCAs	Dry mouth, drowsiness, dizziness, nervousness, constipation	Contraindicated with MAOIs; can cause seizures; use with caution in patients with cardiovascular disease and in those receiving sympathomimetics, anticholinergics, and thyroid hormone
Dopamine reuptake inhibitor			
Bupropion, 300–450 mg (75–225 mg)	Less weight gain, fewer adverse effects on sexual functioning; approved for smoking cessation	Lowers seizure threshold, may exacerbate eating disorders, anorexia, dry mouth, rash, sweating, tinnitus, tremor, abdominal pain, agitation, anxiety, dizziness, insomnia, myalgia, nausea, palpitation, pharyngitis, urinary frequency	Contraindicated in patients with history of seizures, family history of seizures, and head trauma; missed doses should not be taken with next dose; use with caution with other drugs that may lower seizure threshold and in patients with impaired hepatic function; do not use with MAOIs or in patients with anorexia and bulimia
5-HT_2–receptor agonist			
Nefazodone, 200–600 mg	Fewer adverse effects on sexual functioning; lower incidence of postural hypotension than TCAs but higher than that of SSRIs; low incidence of clinically significant ECG abnormalities	Liver failure in 1/250,000–300,000 patient-years; somnolence, dry mouth, nausea, dizziness, constipation, asthenia, lightheadedness, blurred vision, confusion, abnormal vision	Contraindicated with terfenadine, astemizole, cisapride, pimozide, or carbamazepine; do not use with triazolam, and alprazolam; use with caution in cardiovascular, cerebrovascular, and seizure disorders; drug removed from European market because of risk for liver failure
TCA			
Nortriptyline, 25–150 mg (10–100 mg) Desipramine, 25–300 mg Amitryptyline, 25–300 mg Doxepin, 25–300 mg Imipramine, 25–300 mg Amoxapine, 50–300 mg Clomipramine, 25–250 mg Protriptyline, 15–60 mg Trimipramine, 50–300 mg	Desipramine least sedating Amitryptyline and doxepin may be taken at bedtime to aid with sleep	Dry mouth, dizziness, nervousness, constipation, nausea, sedation, anticholinergic and orthostatic hypotension, may cause tardive dyskinesia and the neuroleptic malignant syndrome	Contraindicated with MAOIs; do not use in patients with prolonged QT interval or drugs that may prolong QT interval; use with caution in patients with cardiovascular disease and arrhythmia and patients prone to urinary retention and on thyroid medications; may precipitate attacks in narrow angle glaucoma; follow ECGs and orthostatic blood pressure changes
MAOI inhibitor, nonselective			
Isocarboxazid, 10–60 mg Tranylcypromine, 20–60 mg Phenelzine, 7.5–90 mg	May be effective when other agents have not been	Dizziness, headache, drowsiness, insomnia, hypersomnia fatigue, weakness, tremors, twitching, myoclonic movements, hyperreflexia, constipation, dry mouth, gastrointestinal disturbances, elevated serum aminotransferases (without accompanying signs and symptoms), weight gain, postural hypotension, edema, sexual disturbances	Contraindicated in patients with cerebrovascular and cardiovascular disease, pheochromocytoma, liver disease; increases risk for hypertensive crisis and serotonin syndrome (hypertension, hyperthermia, tachycardia, death); many dietary (tyramine-containing foods) restrictions; interactions with many prescription and OTC drugs, also with alcohol, barbiturates, and cocaine; infrequently used in primary care; extensive patient education and caution in using with other medications are required

** Doses for geriatric patients are in parentheses. ECG = electrocardiogram; FDA = U.S. Food and Drug Administration; GI = gastrointestinal; MAOI = monoamine oxidase inhibitor; OTC = over the counter; SNRI = serotonin and noradrenaline reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant.*

restrictions and potential for hypertensive crisis. However, MAOIs may be more effective in patients with atypical depression (characterized by hypersomnolence, hyperphagia, and rejection sensitivity) (40). Primary care clinicians should consult with a psychiatrist before considering MAOI therapy.

In contemporary practice, TCAs are also used less often because they may cause intolerable dry mouth, constipation, and dizziness and are relatively contraindicated in patients with coronary artery disease, congestive heart failure, and arrhythmias.

There are no important clinical differences in response rates among commonly prescribed antidepressants (including SSRIs, bupropion, duloxotine, mirtazapine, and venlafaxine) (41). Drug selection is based on tolerability, safety, evidence of effectiveness with the patient or first-degree relative, and cost. Regardless of the drug, therapy is effective. Within approximately 6 weeks, half of persons receiving antidepressants have at least a 50% reduction in symptoms (42).

How should clinicians monitor response to drug therapy?

Treatment for depression requires a minimum of 6 to 9 months of close follow-up. The first 2 weeks of drug therapy is often the most challenging for patients. The pessimism and hopelessness intrinsic to depression and the relatively rapid onset of adverse effects can lead to nonadherence: 28% of depressed primary care patients stop taking their medication during the initial month of treatment, and 44% stop within 3 months (43).

Clinicians should follow-up with patients within 1 to 2 weeks of initiation of therapy to ask about acceptance of medication, reinforce educational messages, reassess suicidality, and address adverse events. Telephone follow-up by a trained nurse is also effective (44). Addressing specific adverse effects as they emerge is critical to helping patients continue medication until they respond. In addition, antidepressants may be associated with an increased risk for suicide in children, adolescents, and young adults.

A meta-analysis of 2741 patients age 6 to 18 years showed an increased relative risk for self-harm or suicide-related events among patients treated with newer-generation antidepressants compared with those given placebo (4.8% vs. 3.0%; P = 0.01; number needed-to-treat for harm, 55) (45).

The U.S. Food and Drug Administration (FDA) has issued a Public Health Advisory recommending close monitoring of all patients treated with antidepressants, particularly early in the course of treatment. A warning statement regarding a possible increased risk for suicide has been added to FDA Patient Information Sheets for citalopram, duloxetine, venlafaxine, escitalopram, fluvoxamine, paroxetine, fluoxetine, miratzapine, bupropion, and sertraline. However, the preponderance of evidence suggests that when properly administered, antidepressants avert many more suicides than they cause (46).

During the next 12 weeks, patients should be monitored in person or by phone on a monthly basis. Clinicians can use these encounters to assess adherence to medication and psychotherapy, emergence of adverse effects, symptom breakthrough, suicidality, and psychosocial stress.

Clinicians can also use a structured instrument, such as the PHQ-9, to assess changes in symptom severity by following changes in the score over time: A 50% decrease in symptoms constitutes an adequate response; a 25% to 50% response may indicate the need to modify treatment.

Recurrence of depression after a first episode is common. Clinicians should educate patients and their families to self-assess for symptoms and risk for recurrent episodes. Surveillance for recurrence or relapse should continue indefinitely.

Drug therapy for depression requires a minimum of 6 to 9 months with close follow-up.

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44. Wells KB, Sherbourne C, Schoenbaum M, et al. Impact of disseminating quality improvement programs for depression in managed primary care: a randomized controlled trial. JAMA. 2000;283:212-20. [PMID: 10634337]

Consider long-term maintenance therapy for patients who have had 3 depressive episodes.

How long should clinicians treat depressed patients with drugs and when should they consider long-term maintenance on drug therapy?

The aim of therapy is complete remission of symptoms and return to normal functioning. In first episodes, treatment with antidepressant medication should be continued for 4 to 9 months after remission is achieved. Treatment to remission may take 1 to several months. While not strictly evidence-based, some clinicians advocate treatment for 1 year to maintain remission during 1 occurrence of every major holiday and anniversary. For patients with a history of depressive episodes, many experts advocate a "three-strikes-and-you're-on" strategy, meaning that after 3 depressive episodes, long-term maintenance therapy is recommended (47).

When should clinicians consider switching drugs because of a suboptimal response to initial drug therapy?

A minority of patients starting antidepressant therapy achieve complete remission, and increasing the dosage of the current medication or changing drugs is often necessary.

The STAR-D study randomly assigned 4041 patients to one of several treatment sequences, all starting with 12 weeks of citalopram. This landmark trial showed that 1) 30% of patients achieved complete remission after 12 weeks of treatment with citalopram; 2) of those in whom the first antidepressant failed, about 25% responded to a second alternative agent (sertraline, venlafaxine, or bupropion); 3) about one third of patients not achieving remission with citalopram responded to augmentation with bupropion (48).

The main message to clinicians and patients is not to give up, as both substitution and augmentation strategies may eventually be effective.

Complete intolerance or nonresponse should be addressed by a change in medication. Intolerance and lack of response to any particular antidepressant are common but not predictive of response to another antidepressant (49).

If response to treatment is not complete by week 6, clinicians have several treatment options (Table 6). If a partial response is observed, the dose of the initial agent should be maximized as tolerated before the medication is switched or another is added. If partial response continues, introduction of a second drug while maintaining the initial agent can be tried.

The advantages of combination therapy include faster effect than when 1 medication is withdrawn and another is started, potential for synergistic or complementary effect, and avoidance of withdrawal symptoms when the first agent is stopped. The disadvantages include the increased complexity of the regimen, increased opportunities for drug interactions, and adverse effects.

The addition of bupropion to an SSRI or venlafaxine therapy may enhance response or treat side effects in many patients (50). Similar response rates are found when adding mirtazapine to SSRI treatment (51). Combinations of MAOIs and either SSRIs or TCAs are not recommended because they may trigger the serotonin syndrome (marked by confusion, nausea, autonomic instability, and

Table 6. Treatment Options for Incomplete Response to Therapy*

Increase dose of the current medication
Switch to a different antidepressant
Add a second antidepressant (combination therapy; for example, an SSRI plus bupropion, a TCA, or mirtazapine)
Add an agent not typically used for depression (psychiatric consultation advised), e.g., lithium, liothyronine, risperidone, or pindolol
Add psychotherapy

** SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant.*

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48. Trivedi MH, Fava M, Wisniewski SR, et al. Medication augmentation after the failure of SSRIs for depression. N Engl J Med. 2006;354:1243-52. [PMID: 16554526]

hyperreflexia). There are no controlled studies of the use of stimulants (e.g., methyphenidate, dextroamphetamine) for augmentation (52). Adding psychotherapy to pharmacotherapy is another option.

What are the common adverse effects of antidepressant drugs and how should clinicians manage these effects?

Some specific side effects are more common with particular drugs and should guide choice of replacement medication (Table 5). Sexual side effects of SSRIs include decreased libido or interest (men and women), anorgasmia (women), and delayed ejaculation (men). Strategies for addressing these side effects include pretreatment counseling, switching to a drug with a different mechanism of action (e.g., bupropion or mirtazapine), or augmenting with sildenafil for SSRI-associated erectile dysfunction in the absence of contraindications (53). Switching to bupropion may also be helpful in patients who experience undesired weight gain. Agitation or excessive activation, seen most commonly with fluoxetine, warrants switching to another SSRI or adding a low-dose tricyclic agent or mirtazapine. During SSRI initiation, some clinicians provide a short course of benzodiazepines to counter short-term agitation.

When should clinicians consult a psychiatrist for help in managing drug therapy?

Treatment-resistant depression is a common clinical problem that may necessitate psychiatric consultation. Patients who have not responded to agents familiar to the primary care provider, who have experienced repeated failures, or who have side effects that are difficult to control should be referred for psychiatric consultation. The threshold for referral should be lower for more severely impaired patients. The Agency for Health Care Policy and Research recommends referral to a psychiatrist if the patient has severe symptoms, such as suicide risk; comorbid medical, psychiatric, or substance abuse problems; and lack of response to appropriate treatment (21).

Electroconvulsive therapy can be considered as first-line treatment for depressed patients with psychotic features, those with active suicidal thoughts, or those who have not responded to or who cannot tolerate antidepressants. Electroconvulsive therapy should be managed by a psychiatrist (4).

When should clinicians consider hospitalizing depressed patients?

Hospitalization is usually necessary when suicidal intent is significant but may also be warranted for suicidal ideation alone. Clinicians should consider hospitalization for patients: 1) with significant suicidal ideation or intent who do not have adequate safeguards in their family environment; 2) who express intent to hurt others; 3) who require close observation (to assess ability for self-care and adherence); 4) who are in need of detoxification or substance abuse treatment; 5) who are candidates for electroconvulsive therapy; or 6) who have dysfunctional family systems potentially exacerbating their depressive disorder or interfering with treatment. When life is in jeopardy, patients may be hospitalized against their wishes. The conditions of involuntary hospitalization are governed by legal requirements for corroborated documentation of risk and judicial review.

What should clinicians advise patients about complementary–alternative treatments for depression?

St. John's wort may be beneficial for patients who want to take something for subsyndromal depression or who are unwilling or cannot take conventional therapy for mild depression. St. John's wort has not been shown to benefit patients with moderate to severe major depression and is not indicated in these situations. Although St. John's wort has produced mixed results when studied in randomized, placebo-controlled trials, serious adverse effects are uncommon. Many trials with positive findings have used standardized doses of 0.3% hypericin, 300 mg three times a day (54).

There are several important caveats to the use of St John's wort. To avoid

Recognize the need for psychiatric consultation and/or hospitalization for patients with severe disease, treatment nonresponders, and those with suicidal ideation.

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52. Nelson JC. Augmentation strategies in depression 2000. J Clin Psychiatry. 2000;61 Suppl 2:13-9. [PMID: 10714619]

Patients with recurrent depression should be carefully evaluated for long-term maintenance therapy.

symptoms of serotonin excess, it should not be used in conjunction with SSRIs. Through activation of the cytochrome P450 system, St. John's wort may reduce plasma concentration of such drugs as digoxin, theophylline, simvastatin, and warfarin (55). Severe drug interactions have also been reported with antiretroviral therapy; St. John's wort can decrease concentrations of protease inhibitors and nonnucleoside reverse transcriptase inhibitors (56). At high concentrations, St. John's wort has been shown to be harmful to sperm cells and may lead to decreased fertility (57). The National Institute of Health's National Center for Complementary and Alterative Medicine is a good resource for more information (http://nccam.nih.gov/health/stjohnswort).

If a patient relapses after cessation of depression treatment, should clinicians resume previously effective therapy or select a new therapy?

Recurrence of major depression should be treated with long-term maintenance therapy with the same antidepressant therapy that previously led to remission. Clinicians should consider lifetime maintenance therapy for patients who have had 3 or more episodes and for patients with a first recurrence and risk factors for further recurrences (family history of bipolar disorder, recurrence within 1 year, onset in adolescence, severe depression, suicidal attempt, and sudden onset of symptoms) (47).

How should clinicians advise women on drug therapy for depression who are or who wish to become pregnant?

The FDA has issued a warning concerning SSRI use during pregnancy (58). A case–control study showed that persistent pulmonary hypertension (PPHN) was 6 times more common in babies whose mothers took an SSRI after the 20th week of gestation than in babies whose mothers did not take an antidepressant (59). The absolute risk for PPHN was low (about 6 to 12 per 1000 women). However, this study adds to concerns from previous reports that infants of mothers taking SSRIs late in pregnancy may have such problems as irritability; difficulty feeding; and in very rare cases, difficulty breathing.

The teratogenic potential of SSRIs is probably low overall, but 2 epidemiologic studies of paroxetine in early pregnancy prompted the FDA in late 2005 to order a change in labeling for this agent (www.fda.gov/cder/drug/advisory/paroxetine200512.htm). Paroxetine is the only SSRI with a class D rating for pregnancy; all others are class C. On the other hand, stopping antidepressants carries its own risks.

In a study of 201 pregnant women with a history of major depression before pregnancy, relapse of depression was more common among those who stopped their medication compared with those who maintained their medication (68% vs. 26%, hazard ratio 5.0, $P < 0.001$) (60).

Tricyclic antidepressants are not strictly contraindicated in pregnancy. However, the neonatal withdrawal syndrome may occur, and these drugs should be tapered before delivery (47). If a TCA is chosen, desipramine or nortriptyline may be preferred because they cause fewer side effects and drug levels can be monitored (61). Clinicians should help patients make an informed decision and remember to monitor for signs of postpartum depression 4 to 6 weeks after delivery.

CLINICAL BOTTOM LINE

Treatment... Primary care physicians play an increasingly important role in treating affective disorders. Depression is highly treatable and has many treatment options; clinicians familiar with 2 SSRIs, bupropion, and an SNRI (such as venlafaxine) are well equipped to treat most cases. Familiarity with local psychotherapy options is also helpful.

53. Nurnberg HG, Hensley PL. Selective phosphodiesterase type-5 inhibitor treatment of serotonergic reuptake inhibitor antidepressant-associated sexual dysfunction: a review of diagnosis, treatment, and relevance. CNS Spectr. 2003;8:194-202. [PMID: 12595814]
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What can clinicians do to encourage adherence to therapy for patients with depression?

Patient education is the first line of defense against nonadherence to antidepressant therapy.

In 1 study of 155 depressed patients, those who received the following educational messages were more likely to comply with therapy during the first month: 1) take the medication daily; 2) antidepressants must be taken for 2 to 4 weeks for a noticeable effect; 3) continue to take medicine even if feeling better; 4) do not stop taking antidepressant medication without checking with the physician; 5) resolve questions regarding antidepressants and potential side effects with the physician (43) .

Nonadherence often begins in the initial weeks of therapy. Reasons for nonadherence can include beliefs about the illness, concerns over side effects, ineffectiveness of treatment, cost of medications, and many other cultural and attitudinal factors (62). Clinicians should routinely ask patients and their families about their beliefs. Personalizing educational messages to the patient's actual beliefs will enhance the effect of patient education. When possible, family involvement may improve acceptance of and support for the patient's problems and enhance treatment. Clinicians should provide patients and their families with appropriate written and electronic patient education materials about depression and its management. Clinicians can improve the impact of printed material by intensive reinforcement of key educational messages (43).

Improving outcomes in depression care requires systems change. Evidence suggests that it is more likely that screening will actually take place if initiated by an automatic, nonphysician-triggered procedure (e.g., by nursing staff automatically assessing patients at visit entry rather than by procedures that rely on the physician's decision to initiate screening). Disease management "care pathways" address the multiple needs of patients with depression throughout the course of the illness. Programs that include coordination of care by care managers, provider education and feedback on performance, structured systematic assessment of patient response to treatment with feedback to the provider, stepped-care referrals for psychiatric consultation based on structured systematic assessment of patient progress, nurse-administered telephone support and education calls, or peer support are superior to usual care (2, 44).

What criteria are used to judge the quality of depression care?

In the era of quality performance, the AQA alliance has adopted 2 antidepressant medication management measures developed by the National Committee for Quality Assurance: antidepressant therapy for at least 12 weeks after the initial diagnosis and treatment; and continuous antidepressant therapy for at least 6 months after the initial diagnosis and treatment. For more information, see www.aqaalliance.org/performancewg.htm.

What do professional organizations recommend regarding screening for and managing depression?

In 2002, the United States Preventive Services Task Force issued guidelines on screening for depression (www.ahrq.gov/clinic/uspstf/uspsdepr.htm). The Task Force recommends screening adults in clinical practices that have systems in place to ensure accurate diagnosis, effective treatment, and follow-up. It does not recommend screening children or adolescents. The Task Force's guidelines are currently being updated. The Task Force also issued a guideline on screening for suicide risk in 2004 (www.ahrq.gov/clinic/uspstf/uspssuic.htm).

Patient education is the first line of defense against nonadherence to antidepressant therapy.

58. FDA Public Health Advisory: Treatment Challenges of Depression in Pregnancy. Rockville, MD: U.S. Food and Drug Administration; 2006.
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60. Cohen LS, Altshuler LL, Harlow BL, et al. Relapse of major depression during pregnancy in women who maintain or discontinue antidepressant treatment. JAMA. 2006;295:499-507. [PMID: 16449615]
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The American Psychiatric Association published its Practice Guideline for the Treatment of Patients with Major Depressive Disorder in 2002, which contains useful algorithms for initial choice of treatment method and information on antidepressant medications (www.psych.org/psych_pract/treatg/pg/MDD2e_05-15-06.pdf). Updates to this guideline were published in 2005 (www.psych.org/psych_pract/treatg/pgMDD.Watch.pdf).

The MacArthur Initiative in Depression and Primary Care, in collaboration with Dartmouth College and Duke University, has expanded the work of the AHRQ and provides a comprehensive Web site that includes provider guidelines and patient education resources covering all aspects of depression management. It can be accessed at www.depression-primarycare.org.

Pharmacologic therapy of major depression and dysthymia is covered in clinical guidelines issued in 2000 from the ACP (www.annals.org/cgi/content/full/132/9/738).

in the clinic

Tool Kit

Depression

Depression Screening Instruments

www.chcr.brown.edu/pcoc/cesdscale.pdf
Center for Epidemiological Studies Depression Scale

http://healthnet.umassmed.edu/mhealth/ZungSelfRatedDepressionScale.pdf
Zung Self-Depression Scale

www.stanford.edu/~yesavage/GDS.html
Geriatric Depression Scale

www.nelmh.org/downloads/other_info/hopkins_symptom_checklist.pdf
Hopkins Symptom Checklist

www.aap.org/practicingsafety/Toolkit_Resources/Module2/EPDS.pdf
Edinburgh Postnatal Depression Scale

The American College of Physicians' PIER Depression Module

http://pier.acponline.org/physicians/public/d954/d954.html
PIER (the Physicians' Information and Education Resource) is an evidence-based, electronic resource for clinical recommendations and links to patient information materials at the point of care.

Pamphlet from the American College of Physicians

www.doctorsforadults.com/images/healthpdfs/depression.pdf
Downloadable brochure on depression and how internists can help.

MacArthur Initiative on Depression

www.depression-primarycare.org
Patient education handouts on depression symptoms, management, medications, and psychological counseling.

Patient Information Sheet

www.annals.org/intheclinic/tools
Download an electronic copy of the patient information sheet on the next page for duplication and use in your office

MedlinePLUS Depression Materials

www.nlm.nih.gov/medlineplus/depression.html
Public-oriented information on depression, including educational information from the National Institutes of Mental Health and other organizations, recent studies, and news. Many resources are available in Spanish.

Things People Should Know about Depression

HEALTH TiPS*

Depression makes you feel sad and makes it hard to do or enjoy anything. Talking to a therapist or taking the right medicine can make you feel better.

What You Can Do

- Don't be afraid to ask for help.
- If the doctor gives you medicine, take it every day.
- Don't expect your medicine to work for 2 to 4 weeks after you start it.
- Keep taking your medicine even if you feel better.
- Don't stop your medicine without checking with your doctor.
- Expect to take your medicine for at least 6 months.

See the doctor 1 to 2 weeks after you start medicine and then again in 6 weeks.

Ask your doctor about side effects--putting on weight, feeling nervous or having trouble with sex.

Ask your doctor about the right people to talk to and how your family can help you.

If you feel bad or need help, call your doctor or 911 or go to the emergency room right away.

Ask your doctor about seeing a specialist if:

- ❑ Your medicines don't seem to be working
- ❑ Your medicines have too many side effects
- ❑ You are having strange thoughts or big mood swings
- ❑ You feel you may hurt yourself or other people
- ❑ You are drinking too much or taking street drugs

The next visit with the doctor is _____

*HEALTH TiPS are developed by the American College of Physicians Foundation and PIER.

Web Sites with Good Information about Depression

MedlinePLUS
www.nlm.nih.gov/medlineplus/depression.html

National Alliance on Mental Illness
www.nami.org/Template.cfm?Section=By_Illness&Template=/TaggedPage/TaggedPageDisplay.cfm&TPLID=54&ContentID=23039

National Institutes of Mental Health
www.nimh.nih.gov/publicat/depression.cfm

U.S. Food and Drug Administration
www.fda.gov/fdac/features/2003/103_dep.html

National Cancer Institute (Spanish)
www.cancer.gov/espanol/pdq/cuidados-medicos-apoyo/depresion/patient/

CME Questions

MKSAP
MEDICAL KNOWLEDGE Self-Assessment Program

1. A 37-year-old woman is evaluated for major depression that was diagnosed 1 month ago and treated with fluoxetine. Two weeks after treatment, she had no suicidal ideation, and her depressive symptoms improved, with a 5-point decrease in her PHQ-9 score. During today's visit, she reports that her depressive symptoms have continued to improve, although she has experienced sexual dysfunction manifested by anorgasmia. Her medical history includes hypertension, for which she takes hydrochlorothiazide and lisinopril.

   On physical examination, body mass index is 29 and blood pressure is 146/90 mm Hg. The remainder of the examination is normal.

   Which of the following is the most appropriate alternative treatment option for this patient?

   A. Citalopram
   B. Mirtazapine
   C. Venlafaxine
   D. Bupropion
   E. Sertraline

2. A 38-year-old woman is evaluated because she thinks she might be depressed. She reports feeling tired all the time and sometimes cries with little provocation. She denies anhedonia, problems with sleeping or appetite, suicidal ideation, psychomotor retardation, or problems with concentration. She has 2 children, ages 4 and 2 years, and finds motherhood both frustrating and rewarding. She sometimes feels guilty because she works part-time and believes that she has failed to meet her end of the family's financial responsibilities. Her medical history is noncontributory. She takes no medications except for a multivitamin. She drinks 1 glass of wine on most evenings and does not use illicit drugs.

   On physical examination, she appears well groomed, alert, and oriented. The remainder of the physical examination is unremarkable. Laboratory studies, including complete blood count, serum electrolyte, creatinine, blood urea nitrogen, and thyroid-stimulating hormone levels, and urinalysis, are normal.

   Which of the following is the most appropriate management option for this patient?

   A. Paroxetine
   B. Follow-up monitoring
   C. Psychotherapy
   D. Clonazepam
   E. Quetiapine

3. A 29-year-old woman is evaluated during a follow-up visit for recurrent bouts of depression that she has been having for about 7 years and for which she has taken antidepressants. Her depression has been well-controlled with sertraline, and she denies feeling depressed or experiencing anhedonia on this visit. She has been considering going back to graduate school but finds she is too embarrassed to do so because she has always found it difficult to go out in public and avidly avoids being the center of attention. She also reports having nightmares in which she attends class in her underwear or trips and falls in front of the whole class. The patient does not use alcohol but reports that her father was an alcoholic.

   The physical examination is unremarkable. Laboratory studies, including complete blood count, liver chemistry and renal function tests, serum electrolyte and thyroid-stimulating hormone levels, and urinalysis, are normal.

   In addition to cognitive behavioral therapy, which of the following is the most appropriate treatment option for this patient?

   A. Add clonazepam
   B. Increase sertraline
   C. Taper sertraline over the next 2 weeks
   D. Substitute paroxetine for sertraline

4. A 75-year-old woman is evaluated for symptoms of urinary incontinence that have increased gradually over the past several months. She notes the frequent urge to urinate and has difficulty controlling her urine flow. She now wears pads in the daytime and at night. She lives alone and is able to care for herself. A few months ago, she was diagnosed with depression and began taking nortriptyline. Her medical history is significant for a hysterectomy for fibroid tumors and hypertension that has been well-controlled with nifedipine and atenolol for several years.

   On physical examination, the pulse rate is 65/min and blood pressure is 125/82 mm Hg. The pelvic examination reveals atrophy of the vaginal tissues and the absence of a uterus and cervix. Results of urinalysis are normal.

   Which of the following is the most appropriate next step in the management of this patient?

   A. Replace nortriptyline with another class of antidepressant
   B. Replace atenolol with another class of antihypertensive agent
   C. Replace nifedipine with another class of antihypertensive agent
   D. Begin oxybutynin
   E. Begin oral estrogen therapy

5. A 45-year-old woman is evaluated for a 1-year history of almost-daily exhaustion and difficulty performing daily functions. Her symptoms are exacerbated by physical effort and performing complex cognitive tasks that she had previously been fully capable of doing. Although she reports chronic low levels of energy, she has not had any sleep disturbances, daytime somnolence, spousal reports of snoring, depressed mood, anhedonia, or excessive life stressors. She takes no medications except for periodic use of psyllium. Her medical history is significant for the irritable bowel syndrome. She has been evaluated by several other physicians since the onset of her fatigue and has undergone extensive work-ups to rule out cancer; such work-ups included colonoscopy, mammography, Papanicolaou testing, and cardiopulmonary evaluation. The results have all been normal.

   On physical examination, her vital signs are normal. Body mass index is 26. Cardiopulmonary examination is unremarkable, and laboratory studies, including complete blood count, erythrocyte sedimentation rate, and serum thyroid-stimulating hormone level, are normal.

   Which of the following is the most appropriate next step in the management of this patient?

   A. Cognitive behavioral therapy
   B. Fluoxetine
   C. Galantamine
   D. Hydrocortisone plus fludrocortisone

Questions are largely from the ACP's Medical Knowledge Self-Assessment Program (MKSAP). Go to www.annals.org/intheclinic/ to obtain up to 1.5 CME credits, to view explanations for correct answers, or to purchase the complete MKSAP program.