

# Depression in Later Life: A Diagnostic and Therapeutic Challenge

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Depression in elderly persons is widespread, often undiagnosed, and usually untreated. The current system of care is fragmented and inadequate, and staff at residential and other facilities often are ill-equipped to recognize and treat patients with depression. Because there is no reliable diagnostic test, a careful clinical evaluation is essential. Depressive illness in later life should be treated with antidepressants that are appropriate for use in geriatric patients. A comprehensive, multidisciplinary approach, including consideration of electroconvulsive treatment in some cases, is important. The overall long-term prognosis for elderly depressed patients is good. (*Am Fam Physician* 2004;69:2375-82. Copyright © 2004 American Academy of Family Physicians.)

**D**epression is not a normal part of aging.<sup>1</sup> The lack of connection between health care and mental health providers has created a fragmented system of care for depressed elderly patients that is often inadequate.<sup>2</sup> Concurrent medical problems and lower functional expectations of elderly patients often obscure the degree of impairment.<sup>3</sup> Typically, elderly patients with depression do not report depressed moods but instead present with less specific symptoms such as insomnia, anorexia, and fatigue. Elderly persons sometimes dismiss less severe depression as an acceptable response to life stress or a normal part of aging. Depression costs \$43 billion annually in the United States, in direct and indirect costs—about the same as coronary heart disease.<sup>2</sup>

## Epidemiology

### MAJOR DEPRESSION

Nearly 5 million of the 31 million Americans who are 65 years or older are clinically depressed, and 1 million have major depression.<sup>4</sup> The prevalence of depression in the total U.S. population is 1 percent (1.4 percent in women, 0.4 percent in men), and the rate approaches 12 to 30 percent in patients who live in long-term care facilities.<sup>5</sup> Depression has been identified in 17 to 37 percent of elderly patients treated in primary care settings; of these patients, about 30 percent have been diagnosed with major depression.<sup>1</sup>

Approximately 3 percent of healthy elderly persons living in the community have major depression,<sup>6</sup> and 75 percent initially present to a primary care physician.<sup>4</sup>

Recurrence may be as high as 40 percent. Suicide rates are nearly twice as high in depressed patients as in the general population.<sup>5</sup> Sixty-three percent of persons who commit suicide are white, elderly men, and 85 percent of them have an associated psychiatric or physical illness.<sup>7</sup> Approximately 75 percent of elderly persons who commit suicide had visited a primary care physician within the preceding month, but their symptoms were not recognized or treated.<sup>7-9</sup> Depression is the most common diagnosis in older persons who commit suicide; in younger persons who commit suicide, the most common diagnoses are substance abuse and psychosis, alone or in combination with a mood disorder.<sup>1</sup>

Risk factors for depression in elderly persons include a history of depression, chronic medical illness, female sex, being single or divorced, brain disease, alcohol abuse, use of certain medications, and stressful life events.<sup>4</sup> Up to 15 percent of widowed adults have potentially serious depression for a year or longer after the death of a spouse.<sup>4</sup>

Unlike younger persons with depression, elderly persons with depression usually have a medical comorbidity.<sup>9,10</sup> Major depression is more common in medically ill patients who are older than 70 years and hospitalized or institutionalized.<sup>4</sup> Severe or chronic diseases

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TABLE 1  
Geriatric Depression Scale

Are you basically satisfied with your life? (no)	Do you feel pretty worthless the way you are now? (yes)
Have you dropped many of your activities/interests? (yes)	Do you worry a lot about the past? (yes)
Do you feel that your life is empty? (yes)	Do you find life very exciting? (no)
Do you often get bored? (yes)	Is it hard for you to get started on new projects? (yes)
Are you hopeful about the future? (no)	Do you feel full of energy? (no)
Are you bothered by thoughts that you just cannot get out of your head? (yes)	Do you feel that your situation is hopeless? (yes)
Are you in good spirits most of the time? (no)	Do you think that most persons are better off than you are? (yes)
Are you afraid something bad is going to happen to you? (yes)	Do you frequently get upset over little things? (yes)
Do you feel happy most of the time? (no)	Do you frequently feel like crying? (yes)
Do you often feel helpless? (yes)	Do you have trouble concentrating? (yes)
Do you often feel restless and fidgety? (yes)	Do you enjoy getting up in the morning? (no)
Do you prefer to stay home at night, rather than go out and do new things? (yes)	Do you prefer to avoid social gatherings? (yes)
Do you frequently worry about the future? (yes)	Is it easy for you to make decisions? (no)
Do you feel that you have more problems with memory than most? (yes)	Is your mind as clear as it used to be? (no)
Do you think it is wonderful to be alive now? (no)	
Do you often feel downhearted and blue? (yes)	

NOTE: The Geriatric Depression Scale screens for seven characteristics of depression in the elderly: somatic concern, lowered affect, cognitive impairment, feelings of discrimination, impaired motivation, lack of future orientation, and lack of self-esteem. The yes-or-no questionnaire is administered orally, and one point is scored for each answer in parentheses. A score of 10 or more indicates depression (84 percent sensitivity; 95 percent specificity). The sensitivity diminishes in patients with a score of less than 24 on the Mini-Mental State Examination.

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associated with high rates of depression include stroke (30 to 60 percent), coronary heart disease (8 to 44 percent), cancer (1 to 40 percent), Parkinson's disease (40 percent), Alzheimer's disease (20 to 40 percent), and dementia (17 to 31 percent).<sup>4</sup>

#### MINOR DEPRESSION

Minor depression is a clinically significant depressive disorder that does not fulfill the duration criterion or the number of symptoms necessary for the diagnosis of major depression.<sup>11</sup> Minor depression, which is more common than major depression in elderly patients, may follow a major depressive episode. It also can be a reaction to routine stressors in older populations. Fifteen to 50 percent of patients with minor depression develop major depression within two years.<sup>11</sup>

The prevalence of minor depression in the general population ranges from 2.5 to 9.4 percent but significantly increases (to about 47 to 53 percent) in clinical settings.<sup>2,12</sup> About 30 percent of nursing home residents have minor depression, and the female-to-male ratio is 1.3:1.0, compared with a 1.4:0.4 ratio for major depression.<sup>5</sup>

Untreated, the natural course of minor depression is one to two years. Patients with minor depression are less likely to require hospitalization or to commit suicide than patients with major depression, but 51 percent of patients with minor depression report more disability days than persons with major depression.<sup>12</sup> Persons with minor

depression also are more likely to have a concomitant anxiety disorder.

#### Pathophysiology/Pathogenesis

There is evidence of a genetic basis for depression in persons of all ages.<sup>11</sup> There also is substantial evidence that a history of depression is a risk factor for depression later in life. Elderly persons with depression have higher rates of cognitive impairment, cerebral atrophy, enlarged ventricles, leukoencephalopathy, and deep white-matter changes. Left frontal lesions, left lesions of the basal ganglia, and cortical and subcortical atrophy also are common.<sup>13</sup> Medical comorbidity is frequent.

#### Evaluation

The *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed.,<sup>11</sup> gives nine criteria for depression: depressed mood, sleep disturbance, lack of interest or pleasure in activities, guilt and feelings of worthlessness, lack of energy, loss of concentration and difficulty making decisions, anorexia or weight loss, psychomotor agitation or retardation, and suicidal ideation. The presence of at least five of these criteria, occurring nearly every day during the same two-week period, or a score of more than 10 on the Beck Depression Inventory<sup>14</sup> or 10 or more on the Geriatric Depression Scale<sup>15</sup> supports the diagnosis of depression in elderly patients (*Table 1*).

Laboratory tests should include electrocardiography,

TABLE 2

**Medications That May Cause Depression**

<b>Cardiovascular drugs</b>	<b>Antiparkinsonian drugs</b>	<b>Anti-inflammatory/ anti-infective agents</b>	<b>Stimulants</b>
Clonidine (Catapres)	Amantadine (Symmetrel)	Ampicillin	Amphetamines (withdrawal)
Digitalis	Bromocriptine (Parlodel)	Cycloserine (Seromycin)	Caffeine
Guanethidine (Ismelin)	Levodopa (Larodopa)	Dapsone	Cocaine (withdrawal)
Hydralazine (Apresoline)	<b>Antipsychotic drugs</b>	Ethambutol (Myambutol)	Methylphenidate (Ritalin)
Methyldopa (Aldomet)	Fluphenazine (Prolixin)	Griseofulvin (Grisactin)	<b>Hormones</b>
Procainamide (Pronestyl)	Haloperidol (Haldol)	Isoniazid (INH)	Adrenocorticotropin
Propranolol (Inderal)	<b>Sedatives and antianxiety drugs</b>	Metoclopramide (Reglan)	Anabolic steroids
Reserpine (Serpasil)	Barbiturates	Metronidazole (Flagyl)	Glucocorticoids
Thiazide diuretics	Benzodiazepines	Nalidixic acid (NegGram)	Oral contraceptives
<b>Chemotherapeutics</b>	Chloral hydrate	Nitrofurantoin (Furadantin)	<b>Other drugs</b>
6-Azauridine	Ethanol	Nonsteroidal anti-inflammatory agents	Choline
Asparaginase (Elspar)	<b>Anticonvulsants</b>	Penicillin G procaine	Cimetidine (Tagamet)
Azathioprine (Imuran)	Carbamazepine (Tegretol)	Streptomycin	Disulfiram (Antabuse)
Bleomycin (Blenoxane)	Ethosuximide (Zarontin)	Sulfonamides	Lecithin
Cisplatin (Platinol)	Phenobarbital	Tetracycline	Methysergide (Sansert)
Cyclophosphamide (Cytoxan)	Phenytoin (Dilantin)		Phenylephrine (Neo-Synephrine)
Doxorubicin (Adriamycin)	Primidone (Mysoline)		Physostigmine (Antilirium)
Mithramycin (Mithracin)			Ranitidine (Zantac)
Vinblastine (Velban)			
Vincristine			

urinalysis, general blood chemistry screen, complete blood count, and determination of thyroid-stimulating hormone, vitamin B<sub>12</sub>, folate, and medication levels.<sup>1</sup>

Alcohol or substance abuse, certain medications, and physical disorders are associated with depression (*Tables 2 and 3*). Depression must be distinguished from dementia in elderly patients because these conditions share some of the same features (*Table 4*). Older patients, particularly women, may have vegetative symptoms and cognitive dysfunction.<sup>4</sup> Some features that suggest depression include frequent office visits or use of medical services; persistent reports of pain, fatigue, insomnia, headache, changes in sleep or appetite, and unexplained gastrointestinal symptoms; and signs of social isolation and increased dependency. Delayed recovery from a medical or surgical condition, refusal of treatment, and resistance to discharge from a hospital also may be signs of depression.

**Treatment**

Depression is treatable in 65 to 75 percent of elderly patients.<sup>5</sup> Effective management requires a biopsychosocial approach, combining pharmacotherapy and psychotherapy.<sup>16,17</sup> Therapy generally results in improved quality of life, enhanced functional capacity, possible improvement in medical health status, increased longevity, and lower health care costs. Improvement should be evident as early as two weeks after the start of therapy, but full therapeutic effects may require several months of treatment. Recovery from a severe depressive episode usually takes six to 12 months. Studies show that older patients with depression

benefit most from aggressive, persistent treatment.<sup>17</sup> Thus, therapy for older patients should be continued for longer periods than are typically used in younger patients.<sup>1</sup>

**PHARMACOTHERAPY**

Pharmacotherapy for acute episodes of depression usually is effective and free of complications. Underuse or misuse of antidepressants and prescribing inadequate dosages are the most common mistakes physicians make when

TABLE 3

**Physical Disorders Associated with Depression**

Addison's disease	Intracranial tumors (malignant or benign)
Acquired immunodeficiency syndrome	Multiple sclerosis
Angina	Myocardial infarction
Cancer (particularly of the pancreas)	Parkinson's disease
Cerebral arteriosclerosis, cerebral infarction	Pernicious anemia
Cushing's disease	Porphyria
Diabetes	Renal disease
Electrolyte abnormalities (e.g., hypernatremia, hypercalcemia, hypokalemia, hyperkalemia)	Rheumatoid arthritis
Folate and thiamine deficiencies	Senile dementia
Hepatitis	Syphilis
Hypoglycemia	Systemic lupus erythematosus
Hypothyroidism, hyperthyroidism, hyperparathyroidism	Temporal arteritis
Influenza	Temporal lobe epilepsy
	Viral pneumonia

**TABLE 4**  
**Differentiating Dementia and Depression**

<i>Characteristic</i>	<i>Dementia</i>	<i>Depression</i>
Onset	Insidious, indeterminate	Relatively rapid, associated with mood changes
Duration of symptoms	Usually long	Usually short
Orientation, mood, behavior, affect	Impaired, inconsistent, fluctuating	Intact, diurnal variation depressed/anxious, complaints worse than on testing
Cognitive impairment	Consistent; stable or worsening	Inconsistent, fluctuating
Neurologic defects	Often present (e.g., agnosia, dysphasia, apraxia)	Absent
Disabilities	Concealed by patient	Highlighted by patient
Depressive symptoms	Present	Present
Memory impairment	Doesn't remember recent events, often unaware of memory loss. Onset of memory loss occurs before mood change.	Concentration poor, patient complains of memory loss of recent and remote events, follows onset of depressed mood
Psychiatric history	None	Often, history of depression
Answers to questions	Near answers	"Don't know" answers
Performance	Tries hard but is unconcerned about losses	Does not try hard but is more distressed by losses
Associations	Unsociability, uncooperativeness, hostility, emotional instability, reduced alertness, confusion, disorientation	Appetite and sleep disturbances, suicidal thoughts

treating elderly patients for depression. Only 10 to 40 percent of depressed elderly patients are given medication.<sup>17</sup>

Medication is appropriate not only for primary depression but also for depression associated with medical conditions such as cancer, heart and pulmonary diseases, arthritis, stroke, and parkinsonism. However, the physician must consider carefully how the metabolism of the drug may be affected by physiologic changes resulting from aging and other medical problems.<sup>9,18</sup>

**Selective Serotonin Reuptake Inhibitors.** The safety and side effect profiles of selective serotonin reuptake inhibitors (SSRIs) make them the drugs of choice for treating most types of depression (with or without psychotic features).<sup>19</sup> Because dosage adjustments are not required as frequently with these agents as with tricyclic antidepressants or monoamine oxidase inhibitors (MAOIs), fewer office visits are necessary.

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Dropout rates in patients taking SSRIs are generally two thirds to one half those of patients taking tricyclic antidepressants.<sup>19</sup> The potential for a fatal overdose is significantly lower with SSRIs than with tricyclic antidepressants. SSRIs cost more than most other antidepressant agents, but this disadvantage is offset by a decreased need for inpatient and outpatient care. SSRIs have been proved to be as effective as tricyclic antidepressants in controlled clinical trials, with about 70 to 75 percent of patients responding to treatment.<sup>19</sup> Slight improvements in a patient's symptoms may be detected within several days of starting treatment, but two to three months of therapy are necessary to achieve the full benefit of treatment.<sup>20</sup>

SSRIs generally are better tolerated than tricyclic antidepressants and MAOIs, possibly because they have a lower incidence of sedative and anticholinergic effects, little or no influence on cognition when taken in recommended dosages, and fewer adverse cardiovascular effects. Common side effects include weight loss, agitation and insomnia (with fluoxetine [Prozac]), fatigue, dry mouth and constipation (with paroxetine [Paxil]), nausea and diarrhea, headache, and anxiety.

Transitory gastrointestinal side effects may be reduced by slow dosage titration and taking the medication with food. Sexual dysfunction (e.g., decreased libido, delayed ejaculation, inhibited orgasm) occurs in 15 to 30 percent of patients but is less common in patients taking fluvoxamine (Luvox) and the non-SSRIs bupropion (Wellbutrin), mirtazapine (Remeron), and nefazodone (Serzone).<sup>5</sup> A consideration when prescribing fluoxetine is the long half-life of its active metabolite (i.e., four to 16 days), which requires two to three months for elimination. SSRIs are weak

inhibitors of the cytochrome P450 system, and care should be taken when prescribing SSRIs in patients taking drugs that have dosage-dependent enzyme inhibition interactions and a narrow therapeutic index, such as tricyclic antidepressants, neuroleptics, certain antihistamines and anticonvulsants, theophylline, and warfarin (Coumadin).<sup>20</sup>

**Tricyclic Antidepressants.** Most tricyclic antidepressants are thought to be equally effective in elderly and younger patients (Table 5). Tricyclic antidepressants have a long and successful history in the treatment of depression. Some of the most commonly used agents in this class are desipramine (Norpramin) and nortriptyline (Pamelor). These agents have fewer anticholinergic side effects than amitriptyline (Elavil), doxepin (Sinequan), and imipramine (Tofranil), which generally should be avoided in elderly patients. Desipramine is less sedating and can be taken during the day, and nortriptyline is less likely to cause orthostatic hypotension than amitriptyline or imipramine. Daily dosages should start at 10 to 20 mg per day and be raised every week by 10 to 20 mg.<sup>18</sup>

Compared with younger patients, a significant response to therapy often occurs later in elderly patients taking tricyclic antidepressants, commonly after six to 12 weeks of therapy. Dosage compliance is important in elderly patients but may be difficult to achieve. Lack of adherence to instructions results in wide fluctuations in plasma drug levels, which have been shown to predict poor outcomes.<sup>5</sup>

The measurement of plasma drug levels is an important management tool in elderly patients who have limited or no response to therapy or a history of organ impairment, who are taking multiple medications, or whose dosage recently has been changed. It also can verify compliance or confirm that therapeutic drug plasma concentrations have been reached.

**Monoamine Oxidase Inhibitors.** Although MAOIs are thought to be dangerous and difficult to use, drugs such as phenelzine (Nardil) are relatively safe and effective in older patients. A full therapeutic response can be achieved after five to seven weeks of treatment. Hypotension, hypertension, and food-drug interactions are the most likely problems with MAOI use. Taking agents from more than one drug class can increase a patient's risk for developing serotonin syndrome (i.e., mental status changes, hyperreflexia, agitation, myoclonus, diaphoresis, shivering, tremor, diarrhea, incoordination, fever)<sup>21</sup> (Table 6).<sup>5</sup>

**Other Antidepressants.** Bupropion may be as effective as tricyclic antidepressants and SSRIs in the treatment of major depression. It now is available in sustained-release

and extended-release preparations, which allow for twice-daily and once-daily dosing, respectively.

A trial of venlafaxine (Effexor) could be considered in elderly patients with treatment-resistant depression. Venlafaxine has a wide dosage range of 75 to 375 mg per day, administered in divided doses two or three times daily. Blood pressure monitoring is necessary in patients with pre-existing cardiovascular disease and patients taking relatively high dosages. Because only 30 percent of the drug is protein bound, drug interactions may be less frequent.

Nefazodone is structurally related to trazodone (Desyrel)<sup>22</sup> and works well in patients with anxiety and depression. Agitation and sexual dysfunction are relatively rare side effects of this agent. Nefazodone also may improve sleep. However, use of nefazodone has been associated with liver failure, and the drug has been taken off the market in Europe and Canada. There are no specific recommendations for monitoring liver functions in patients on nefazodone. Other drawbacks include twice-daily dosing, sedation, and drug interactions.

In elderly patients with psychotic depression, the addition of an antipsychotic medication appears not to reduce relapse or disability, or improve recovery rates.<sup>3</sup>

**Therapeutic Response.** At least two to six weeks of therapy are necessary to achieve a clinical response with all classes of antidepressants. Physicians should reassure patients that they may feel worse before they start to feel better. Only 40 percent of patients have a complete response to the first agent used in therapy; if a patient does not respond to one antidepressant, an agent from a different class should be substituted. If there is at least partial response, a second drug from the same or a different class or a second agent could be added at the lowest dosage that produces a benefit. Monotherapy is preferred, however, because compliance is enhanced and drug interactions and adverse effects are minimized.

Drugs should be discontinued gradually to reduce the risk of unwanted effects such as dizziness, anxiety, headache, and flu-like symptoms. The withdrawal syndrome usually resolves within three weeks.<sup>19</sup> Dosage reduction is not recommended for maintenance therapy; the dosage that originally produced a good response should be continued. Full-dosage maintenance therapy prevents relapse and recurrence in approximately 80 percent of patients.<sup>19</sup>

**Duration of Therapy.** Recurrence risk after the first three episodes of major depression is 50, 70, and 90 percent, respectively.<sup>5</sup> Therapy should be continued for one year after remission from a first episode of depression, at least one to two years after a second episode, and three years

**TABLE 5**  
**Pharmacologic Agents Used to Treat Depression in Elderly Patients**

<i>Drug</i>	<i>Dosage (mg per day)*</i>	<i>Dosing</i>	<i>Cost (generic)†</i>	<i>Common side effects</i>	<i>Interactions</i>
<b>Tricyclic antidepressants (tertiary)</b>					
Amitriptyline (Elavil)‡	25 to 300	Single or divided	\$16 (\$11)	Anticholinergic effects, sedation, cardiac effects, orthostatic hypotension, weight gain, lower seizure threshold	Antiarrhythmics,§ MAOIs§
Imipramine (Tofranil)	25 to 300	Single or divided	48 (1 to 22)	Same as above	Antiarrhythmics,§ MAOIs§
Doxepin (Sinequan)‡	25 to 300	Single or divided	17 (12)	Same as above	Antiarrhythmics,§ MAOIs§
Trimipramine (Surmontil)	25 to 300	Single or divided	32	Same as above	Antiarrhythmics,§ MAOIs§
Clomipramine (Anafranil)	25 to 300	Single or divided	90 (25)	Same as above	Antiarrhythmics,§ MAOIs§
<b>Tricyclic antidepressants (secondary)</b>					
Nortriptyline (Pamelor)	25 to 250	Single or divided	102 (6 to 26)	Same as above	Antiarrhythmics,§ MAOIs§
Protriptyline (Vivactil)	15 to 60	Single or divided	85	Same as above	Antiarrhythmics,§ MAOIs§
Desipramine (Norpramin)	25 to 300	Single or divided	26 (8 to 15)	Same as above	Antiarrhythmics,§ MAOIs§
Amoxapine (Asendin)‡	50 to 600	Single or divided	(30 to 37)	Extrapyramidal movement disorders, male sexual dysfunction, endocrine dysfunction	MAOIs§
<b>MAOIs</b>					
Phenelzine (Nardil)	45 to 90	Divided	49	Orthostatic hypotension	MAOIs,§ meperidine (Demerol),§ vasoconstrictors,§ narcotics,§ decongestants§
Tranylcypromine (Parnate)	30 to 60	Divided	60	Orthostatic hypotension	MAOIs,§ meperidine,§ vasoconstrictors,§ narcotics,§ decongestants§
<b>SSRIs</b>					
Sertraline (Zoloft)	50 to 200	Single	72	GI symptoms, sexual dysfunction, weight gain, headache	MAOIs,§ tricyclic antidepressants, neuroleptics, antiarrhythmics§
Fluoxetine (Prozac)	20 to 80	Single or divided	100 (80)	GI symptoms, anxiety, insomnia, weight loss	MAOIs,§ tricyclic antidepressants, neuroleptics, antiarrhythmics§
Paroxetine (Paxil)	20 to 50	Single	85	GI symptoms, anxiety, insomnia, fatigue	MAOIs,§ tricyclic antidepressants, neuroleptics, antiarrhythmics§
Fluvoxamine (Luvox)	50 to 300	Single	(77 to 89)	GI symptoms, anxiety, insomnia	MAOIs,§ tricyclic antidepressants, neuroleptics, antiarrhythmics,§ antihistamines§
Citalopram (Celexa)	20 to 60	Single	72	GI symptoms, anxiety, somnolence, sexual dysfunction	MAOIs,§ tricyclic antidepressants, neuroleptics, antiarrhythmics,§ antihistamines§
Escitalopram (Lexapro)	10 to 20	Single	67	GI symptoms, anxiety, somnolence, sexual dysfunction	MAOIs,§ tricyclic antidepressants, neuroleptics, antiarrhythmics,§ antihistamines§
<b>Other agents</b>					
Maprotiline (Ludiomil)‡	50 to 225	Single or divided	(22)	Lower seizure threshold	MAOIs§
Bupropion (Wellbutrin)	100 to 450	Divided	42 (29)	Lower seizure threshold	MAOIs§
Trazodone (Desyrel)‡	50 to 600	Single or divided	65 (13)	Sedation, orthostatic hypotension, priapism	MAOIs§
Venlafaxine (Effexor)	75 to 375	Divided	51	Anxiety, sexual dysfunction, increased blood pressure, mild sedation, visual symptoms	MAOIs,§ SSRIs, antihistamines,§ benzodiazepines, neuroleptics
Nefazodone (Serzone)	200 to 600	Divided	36	Same as above	MAOIs,§ SSRIs, antihistamines,§ benzodiazepines, neuroleptics
Mirtazapine (Remeron)	15 to 45	Single	81 (72)	Sedation, increased appetite, constipation, asthenia	MAOIs,§ SSRIs, antihistamines,§ benzodiazepines, neuroleptics

MAOIs = monoamine oxidase inhibitors; SSRIs = selective serotonin reuptake inhibitors; GI = gastrointestinal.

\*—Lower dosage recommended in elderly patients.

†—Estimated cost to the pharmacist for a 30-day supply at the lowest recommended dosage based on average wholesale prices in Red book. Montvale, N.J.: Medical Economics Data, 2004. Cost to the patient will be higher, depending on prescription filling fee.

‡—Not recommended for use in elderly patients.

§—May cause potentially fatal interactions.

TABLE 6  
Drug Monitoring and Contraindications

Medication	Extra monitoring for side effects	Contraindications
Atenolol (Tenormin)	MAOIs, tricyclic antidepressants, trazodone (Desyrel), venlafaxine (Effexor)	
Caffeine	Bupropion (Wellbutrin), fluvoxamine (Luvox), MAOIs, venlafaxine	
Captopril (Capoten)	MAOIs, tricyclic antidepressants, trazodone	
Codeine	Fluoxetine (Prozac), fluvoxamine, paroxetine (Paxil), tricyclic antidepressants, trazodone	MAOIs (hypertensive crisis)
Digoxin	Tricyclic antidepressants	
Nifedipine (Procardia)	MAOIs, nefazodone (Serzone), tricyclic antidepressants	
Phenytoin (Dilantin)	Fluoxetine, fluvoxamine, sertraline (Zoloft)	
Theophylline	Fluoxetine, fluvoxamine, MAOIs	
Tramadol (Ultram)	Citalopram (Celexa), fluoxetine, fluvoxamine, mirtazapine (Remeron), nefazodone, paroxetine, sertraline, tricyclic antidepressants, trazodone, venlafaxine	MAOIs (potentiate seizure risk)
Tricyclic antidepressants	Bupropion, citalopram, fluoxetine, fluvoxamine, mirtazapine, paroxetine, sertraline, trazodone, venlafaxine	MAOIs, tricyclic antidepressants (serotonin syndrome)
Warfarin (Coumadin)	Citalopram, fluoxetine, fluvoxamine, MAOIs, mirtazapine, paroxetine, sertraline, venlafaxine	

MAOIs = Monoamine oxidase inhibitors.

Information from reference 5.

after a third episode.<sup>2</sup> The patient should be seen every month during the first six to 12 months after remission, then every three months after one year of remission.

#### ELECTROCONVULSIVE THERAPY

Electroconvulsive therapy (ECT) is a first-line option in patients with depression and psychotic features who have not responded to antipsychotic and antidepressant medications, and patients with severe nonpsychotic depression who have not responded to adequate trials of two antidepressants. ECT is used most often in patients older than age 60. Patients with delusions, psychomotor retardation, early morning awakening, and a family history of depression are most likely to benefit from ECT.<sup>23</sup> ECT may reverse the memory loss and confusion associated with pseudodementia. Contraindications include recent myocardial infarction, brain tumor, cerebral aneurysm, and uncontrolled heart failure. ECT is an effective short-term therapy but has higher relapse rates over six to 12 months; patients with a history of medication resistance have higher relapse rates following ECT.<sup>23</sup>

#### PSYCHOSOCIAL TREATMENTS

Psychologic therapies are recommended for elderly patients with depression because of this group's vulnerability to adverse effects and high rates of medical problems and medication use.<sup>23</sup> Stressful life events, family conflicts, and the reduction or absence of social support likely will not be affected by medication and other somatic treatment approaches, but patients with these problems are responsive to psychologic intervention.

Psychotherapeutic approaches include cognitive-behavior

therapy, supportive psychotherapy, problem-solving therapy, and interpersonal therapy. The potential benefit of psychotherapy is not diminished by increasing age. Older adults often have better treatment compliance, lower dropout rates, and more positive responses to psychotherapy than younger patients.<sup>23</sup>

The presence and degree of medical comorbidities and cognitive impairment are the main factors affecting the efficacy and success of psychotherapy. Behavior patterns, personality traits, and patients' expectations and preferences about treatment are also predictors of successful psychotherapy. Rather than imposing a new lifestyle, therapeutic conversation uses adaptive strengths that have served the patient well in the past. The psychotherapist and patient should set aside committed and uninterrupted time, focus on increasing the patient's self-esteem, accept feelings at face value, hold out the prospect of hope, and accept anger and irritability. Physical activity should be encouraged, as should social activity (e.g., church and community involvement). Security and self-confidence can be restored through a protective figure such as a physician. Appropriate psychosocial interventions include education (i.e., teaching better coping and adaptation skills), family counseling, participation in bereavement groups, involvement with a senior citizen center, and use of visiting nurse services to help with medication.

Interdisciplinary collaboration should be established in the primary care setting. At minimum, physicians should provide patients and their families with access to adequate information and referrals, preferably in conjunction with senior citizen centers and nutritional programs. Appropriate

TABLE 7

### Indications for Psychiatric Referral in Elderly Patients with Depression

Bipolar disorder	Severely ill
Suicidal ideation	Need for treatment beyond drug therapy
Psychosis	Double depression
Unresponsive or intolerant to adequate trial of first-line treatment	(i.e., episodes of major depression superimposed on dysthymic disorder)
Diagnostically complex or uncertain	
Candidate for electroconvulsive therapy	

ate goals include ongoing evaluation; reduction of depressive symptoms and use of primary care services; and improvement in social and occupational skills, everyday functioning, adaptation and coping skills, work performance, social integration, and quality of life.

### Barriers to Diagnosis and Treatment

Barriers to proper diagnosis and treatment include attributing depressive symptoms to “normal” aging or physical illness, masking the effects of coexisting medical problems, self-medication (e.g., alcohol use), prescription drug use, poverty and low socioeconomic status (which restrict health care access), bereavement, social isolation and lack of family support, misdiagnosis of depression as dementia, hypochondriasis, somatization, cost issues, time constraints, and the stigma associated with mental illness.<sup>2,4</sup> Clinical experience suggests that physicians who look carefully for symptoms of depression rather than relying on the patient to report mood changes have higher rates of recognition and response to therapy.

### Outcome

Many primary care physicians significantly underestimate the extent to which depressed, elderly patients will respond to treatments such as antidepressant medication, psychotherapy, or ECT.<sup>24</sup> The prognosis for recovery is equal in young and old patients, although remission may take longer to achieve in older patients. Most patients (54 to 84 percent) recover, 12 to 24 percent relapse, and 4 to 28 percent remain ill or disabled.<sup>2</sup> In patients with psychotic depression, recovery rates are reduced by one half, and relapse and disability rates are twice those in patients with nonpsychotic depression.<sup>3</sup> Close follow-up and review of side effects are important when prescribing antidepressants because up to 40 percent of patients stop taking prescribed antidepressants within two weeks, and up to 70 percent of patients stop within four weeks.<sup>25</sup>

Table 7 lists reasons to consider referral in elderly patients with depression.

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### REFERENCES

- Alexopoulos G. Pharmacotherapy of depressive disorders in older patients. Minneapolis: McGraw-Hill Healthcare Information, 2001.
- Hirschfeld RM, Keller MB, Panico S, Arons BS, Barlow D, Davidoff F, et al. The National Depressive and Manic-Depressive Association consensus statement on the undertreatment of depression. *JAMA* 1997;277:333-40.
- Meyers BS. Geriatric psychotic depression. *Clin Ger* 1997;5:16-20.
- Boswell EB, Stoudemire A. Major depression in the primary care setting. *Am J Med* 1996;101:3S-9S.
- Alexopoulos GS, Katz IR, Reynolds CF, Carpenter D, Docherty JP. The expert consensus guideline series. Pharmacotherapy of depressive disorders in older patients. *Postgrad Med* 2001. Accessed April 21, 2004, at: <http://www.psychguides.com/Geriatric%20Depression%20LP%20Guide.pdf>.
- Reynolds CF 3d. Depression: making the diagnosis and using SSRIs in the older patient. *Geriatrics* 1996;51:28-34.
- Suicide among older persons—United States, 1980-1992. *MMWR Morb Mortal Wkly Rep* 1996;45:3-6.
- Bruce ML, Leaf PJ. Psychiatric disorders and 15-month mortality in a community sample of older adults. *Am J Public Health* 1989;79:727-30.
- Ganzini L, Smith DM, Fenn DS, Lee MA. Depression and mortality in medically ill older adults. *J Am Geriatr Soc* 1997;45:307-12.
- Callahan CM, Dittus RS, Tierney WM. Primary care physicians' medical decision making for late-life depression. *J Gen Intern Med* 1996;11:218-25.
- American Psychiatric Association. Task Force on DSM-IV. Diagnostic and statistical manual of mental disorders: DSM-IV, 4th ed. Washington, D.C.: American Psychiatric Association, 1994.
- Engel GL. A life setting conducive to illness. The giving-up—give-up complex. *Ann Intern Med* 1968;69:293-300.
- Jones BN, Reifler BV. Depression coexisting with dementia. Evaluation and treatment. *Med Clin North Am* 1994;78:823-40.
- Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry* 1961;4:561-71.
- Yesavage JA, Brink TL, Rose TL, Lum O, Huang V, Adey MB, et al. Development and validation of a geriatric depression screening scale: a preliminary report. *J Psychiatr Res* 1982;83:17:37-49.
- Dunner DL. Therapeutic considerations in treating depression in the elderly. *J Clin Psychiatry* 1994;55 (suppl):48-58.
- Charney DS, Miller HL, Licinio J, Salomon R. Treatment of depression. In: Schatzberg AF, Nemeroff CB, eds. *The American Psychiatric Press textbook of psychopharmacology*. 2d ed. Washington, D.C.: American Psychiatric Press, 1998:575-601.
- Reynolds CF 3d. Treatment of depression in special populations. *J Clin Psychiatry* 1992;53(suppl):45-53.
- Block M, Gelenberg AJ, Malone DA Jr. Rational use of the newer antidepressants. *Patient Care* 1997;31:49-77.
- Bhatia SC, Bhatia SK. Major depression: selecting safe and effective treatment. *Am Fam Physician* 1997;55:1683-94.
- Sporer KA. The serotonin syndrome. Implicated drugs, pathophysiology and management. *Drug Saf* 1995;13:94-104.
- Revicki DA, Brown RE, Palmer W, Bakish D, Rosser WW, Anton SF, et al. Modelling the cost effectiveness of antidepressant treatment in primary care. *Pharmacoeconomics* 1995;8:524-40.
- Nierenberg AA, McColl RD. Management options for refractory depression. *Am J Med* 1996;101:45S-52S.
- Reynolds CF 3d, Frank E, Dew MA, Houck PR, Miller M, Mazumdar S, et al. Treatment of 70(+)-year-olds with recurrent major depression. *Am J Geriatr Psychiatry* 1999;7:64-9.
- Reynolds CF 3d, Frank E, Perel JM, Imber SD, Cornes C, Miller MD, et al. Nortriptyline and interpersonal therapy as maintenance therapies for recurrent major depression. *JAMA* 1999;281:39-45.

Depressive illness in later life should be treated with antidepressants that are appropriate for use in geriatric patients. A comprehensive, multidisciplinary approach, including consideration of electroconvulsive treatment in some cases, is important. The overall long-term prognosis for elderly depressed patients is good.Â Elderly persons sometimes dismiss less severe depression as an acceptable response to life stress or a normal part of aging. Depression costs \$43 billion annually in the United States, in direct and indirect costs about the same as coronary heart disease.<sup>2</sup> Epidemiology MAJOR DEPRESSION. This article exemplifies the AAFP 2004.