Primary Care Issues Related to the Treatment of Depression in Elderly Patients

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Late-life depression is a serious public health problem and a concern for the primary care physician. Illnesses that often occur with aging may present in association with depression, which can interfere with patient compliance and recovery and worsen disease outcomes. Late-life depression is also associated with disproportionately high rates of completed suicide and high mortality rates independent of suicide. A shared therapeutic nihilism exists between many patients and physicians, who inappropriately accept major depression as normal and inevitable during advanced age and with related chronic disease states. Thus, the older depressed patient is too often not diagnosed and not treated. Furthermore, symptom overlap between depression, anxiety, and many chronic medical illnesses may confuse proper diagnosis. Therefore, screening for and diagnosing depression using an inclusive approach is highly recommended in the primary care setting and long-term care facility. Because of their improved safety, tolerability, and ease of dosing, newer generation antidepressants, such as the selective serotonin reuptake inhibitors, should be the first choice of treatment. Collaboration between primary and specialty providers is recommended, and referral to psychiatry is advised for patients with complex medical illnesses, comorbid psychiatric illness, suicidal ideation or intent, complicated medication regimens, and poor or no response to antidepressant therapy.

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Late-life depression remains a substantial public health problem and concern in primary care.[1] Epidemiologic studies summarized by the National Institutes of Health (NIH) Consensus Panel on Diagnosis and Treatment of Depression in Late Life found that 15% of the elderly in community samples had depressive symptoms.[2] Although fewer than 3% had major depression, approximately 5% of elderly patients visiting primary care clinics had minor or major depression.[2] Older patients in nursing homes are particularly at risk for major depression, with a prevalence of 15% to 25% and a 13% incidence of new cases annually.[2]

Despite the high prevalence of geriatric depression, the NIH Consensus Panel concluded that depression is not a normal condition of advanced age and that depression can be distinguished from the normal processes of aging.[2]

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IMPACT OF DEPRESSION

Depression as a Comorbidity

Clinical studies have shown that depression by itself can be as debilitating as many chronic medical illnesses, such as diabetes, arthritis, and hypertension.[3] Often, depression coexists with one or more medical conditions that are associated with aging (Table 1), worsening disease outcomes, increasing the health care burden, and interfering with recovery. Thus, quality of life is diminished and economic burden is increased.

Cardiovascular disease and depression are intimately linked. Chronic cigarette smoking and addiction have been associated with depression and represent a major modifiable cardiovascular risk factor. In major depression, the loss of hypothalamic-pituitary-adrenal homeostasis enhances sympathetic nervous system tone and creates a hypercoagulable state, promoting arrhythmia, coronary artery spasm, and platelet aggregation. This increases the risk of myocardial infarction (MI) and stroke. Depression is prevalent in patients recovering from stroke, ranging from 22% to 30%,[4–8] and it interferes with rehabilitation and resumption of activities.[8–11] One study of patients post-MI found that 18% had major depression and 27% had minor depression.[12] Several investigators have reported that post-MI patients with depression tend to have poorer prognoses and higher mortality rates than those who are not depressed.[12–14]

Table 1. Medical Conditions Frequently Associated With Depression in the Elderly

Condition	Prevalence of Comorbid Depression	Reference
Stroke	22% to 30%	4–8
Myocardial infarction (minor or major)	18%	12
Hip fracture	51%	15
Chronic pain	50%	16

The incidence of depression following surgery for hip fracture was found to be as high as 51%, and patients recovering from hip fracture who are depressed tend to recover less physical and social function.[15]

Depression is estimated to occur in up to 50% of patients with chronic pain.[16] Depression itself can cause pain,[16,17] and treatment for depression can alleviate chronic pain.[18–21] Moreover, compared with patients without depression, patients with depression report more frequent[18,22–25] and more severe[23,26,27] pain. Therefore, it is proposed that treatment of patients with chronic pain should include screening for and treatment of coexisting depression.[28]

Loss of appetite and/or refusal to eat are often related to depression in the elderly and can result in life-threatening malnutrition and weight loss.[29–31] An estimated 10% to 20% of newly admitted elderly nursing home residents lose a clinically significant amount of weight, and approximately 36% of the weight lost among new elderly patients in nursing homes may be due to depression.[31,32] This creates a vicious cycle leading to further frailty, disability, and worsening depression. Antidepressant treatment can improve eating behavior and nutritional intake in the elderly,[33] interrupting this cycle.

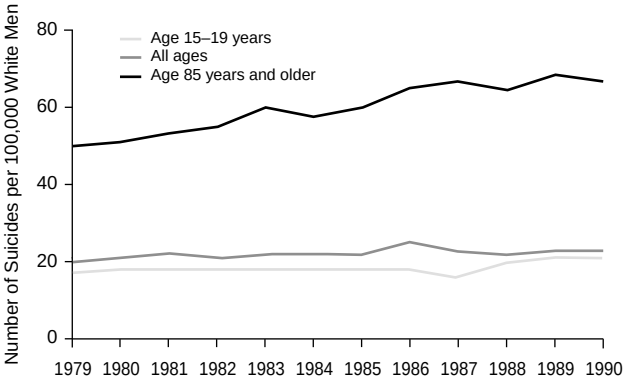
Interference With Medical Treatment

Studies have documented the deleterious effects of depression on adherence to treatment regimens for chronic illnesses, including coronary artery disease and cancer.[34–38] Treatment for comorbid depression can improve patient compliance with medical regimens,[39] improving not only the patient's quality of life, but also disease outcomes.

Physical Decline

Not only does depression increase the burden of medical illnesses and interfere with recovery, it may also hasten physical decline in the elderly, independent of patient health status. In a large-scale study of community-dwelling elderly patients whose physical function and emotional well-being were assessed over a 4-year period, depressive symptoms were predictive of decreases in physical abilities when controlling for other health measures. The authors suggested that treatment of depression may reduce functional decline in the elderly,[40] which is important because functional impairment may precede or predict institutionalization, especially as caregiver burden increases.

Figure 1. Annual Suicide Rates for White Men in the United States Between 1979 and 1990[a]



[a]Data from the National Center for Health Statistics.[106]

Death

For patients with cardiovascular disease,[13,41–44] stroke,[45] or cancer,[38,46] comorbid depression increases the mortality rate. In Japan and Finland, similar relationships between depression and mortality, independent of other health measures, have been documented.[47,48] A study of nursing home patients in the United States found that the likelihood of death was 59% greater for patients who had experienced a major depressive disorder when controlling for other medical conditions.[49]

Although elderly adults comprise only 13% of the population, they represent 25% of suicide attempts, and a suicide attempt made by an elderly person is more likely to result in death than one made by a younger person.[50] Epidemiologic studies have demonstrated that the suicide rate for the elderly is higher than that for the general population. For example, in 1988, the suicide rate for the general population was 12.4 per 100,000, whereas the rate for persons aged 80 to 84 years was 26.5 per 100,000.[2] Elderly white men have the highest rate of suicide.[51–53] According to the National Center for Health Statistics, the suicide rate per year for white men aged 85 years and older in the United States between 1979 and 1990 was consistently more than twice as high as that for all age groups (Figure 1).

Unfortunately, opportunities for preventing suicide are frequently missed in the primary care setting. One retrospective study of elderly patients who had committed suicide found that a majority had visited their primary care physician shortly before their death: 75% within 1 month of committing suicide, 40% within 1 week, and 20% within 24 hours.[54]

Economic Impact

In addition to the medical impact, depression creates an economic burden.[55–57] Patients with depression use more health care services than patients without depression.[58,59]

These services include additional diagnostic tests to investigate somatic complaints, longer hospital stays, and more nursing care hours.[60,61] Depression in combination with other illnesses increases the burden on care providers. For example, 40% of patients with Alzheimer's disease are estimated to have depression. Studies of care providers for patients with Alzheimer's disease have shown that those providing support for patients with coexisting depression have a greater burden of care and an increased likelihood of experiencing distress and/or depression themselves.[62–64]

DIAGNOSIS IN PRIMARY CARE

Failure to diagnose and treat depression in older patients is common. Because of the stigma attached to mental illnesses,[65–70] older patients are often reluctant to report symptoms of depression to their physician. Another reason for the lack of dialogue regarding depressive symptoms in older patients is that neither the patient nor the physician perceives the symptoms of depression as such. A therapeutic nihilism exists between many patients and physicians who inappropriately accept the symptoms of major depression as inevitable or appropriate with chronic medical illness, pain syndrome, aging, or physical or emotional loss. Low Medicare reimbursements (less than 3% of Medicare budget) for mental illness combined with discounted payments to primary care physicians for care associated with a psychiatric diagnosis results in most depressive illness in the elderly being underreported, unrecognized, and untreated in the primary care setting.

Screening for and treating underlying depression in elderly patients, particularly in those with serious illnesses, should be an integral part of primary health care. A study by Chochinov and colleagues[71] tested 4 methods for diagnosis of depression in terminally ill patients against a standard semistructured diagnostic interview for depression: (1) a single question about depressed mood; (2) 2 questions, 1 about mood and 1 about interest in activities; (3) a mood scale based on visual analogs; and (4) the Beck Depression Inventory Short Form. Of the 4 instruments tested, the single-question method ("Are you depressed?") was the most accurate for identifying depression in patients diagnosed as such using the semistructured diagnostic interview. Thus, rather than using elaborate diagnostic scales, the primary care physician can diagnose depression in some elderly patients, particularly those who are terminally ill and not cognitively impaired, with a single question.

Many physicians misinterpret the signs of depression in the older population. The DSM-IV diagnostic criteria for major depression include the presence of at least 4 of the following conditions: weight loss/appetite change, sleep disturbance, psychomotor agitation/retardation, fatigue/loss of energy, feelings of worthlessness or guilt, poor concentration/indecisiveness, and preoccupation with death/suicidal ideation. While the dominant symptoms of depression in the elderly are usually decreased or lost appetite, insomnia, fatigue, weight loss, and tiredness, these symptoms often overlap with and are mistaken for symptoms of other diseases, such as cancer, or the adverse effects of treatments, such as chemotherapy or radiation.[2,66,70,72] In many older patients, simply assessing the patient's mood and looking for common correlates of melancholia may reliably and accurately make a diagnosis of depression. For instance, in addition to the difficulty of accurately assessing depressive symptoms that can manifest as physical symptoms or dementia, the primary care physician attempting to diagnose depression in an older patient may have to deal with hostility and irritability on the part of the depressed patient.[66] Anger and irritability, often associated with anxiety, are a common presentation. Apathy and anhedonia are similarly found as correlates of dysthymia associated with major depressive disorder, but are commonly overlooked. Compounding these difficulties is the limited time generally available to primary care physicians for patient visits.[66]

Physicians who treat older patients may be concerned about correctly distinguishing depression from dementia. Five differential diagnostic points, relating to onset and progression of symptoms, memory characteristics, and circadian influence, allow for distinguishing depression from dementia and are summarized in Table 2.

Regarding dementia, primary care physicians attempting to diagnose depression would be wise to use an inclusive approach. Late-life depression is a known risk factor for the development of dementia and estimates of the prevalence of depression in patients with Alzheimer's disease are at least 40%. Progressive arteriosclerotic cerebrovascular disease is also linked to dementia and depression, and new imaging techniques may be able to link neuropathologic changes to specific depressive symptoms. Most importantly, in dementia, antidepressant treatments, particularly with the selective serotonin reuptake inhibitors (SSRIs), which do not increase anticholinergic burden, have been shown to improve both behavioral and cognitive function. This improvement is often associated with less caregiver burden and may improve the quality of life for both patients and caregivers, thus possibly delaying institutionalization. Because primary care physicians have

Table 2. Distinguishing Characteristics of Depression and Dementia

Characteristic	Depression	Dementia
Onset	Abrupt	Slow
Progression	Rapid	Slow
Memory		
General state	Memory loss	Confabulation
Response to questions	"I don't know"	"Near miss" answers
Circadian influence	Diurnally stable	Sundowning, confusional state

more frequent contact and interaction with older patients compared with specialists, a greater number of opportunities for the diagnosis of depression exist in this setting. Given these opportunities and the importance and benefit of treating depression in the elderly, primary care clinicians treating older patients should adopt an inclusive approach to making this diagnosis. Depression should be ruled out for elderly patients with underlying chronic medical illness rather than ruled in.

PRIMARY CARE TREATMENT OF DEPRESSION IN ELDERLY PATIENTS

Given the heterogeneous nature of late-onset depression, many obstacles can interfere with full recovery from depression in older patients. Underlying chronic medical illness and pain, neurodegenerative changes and dementia, adverse life events, inadequate family supports, secret self-medication, substance abuse, bereavement, interpersonal conflicts, and social isolation can directly interfere with adherence to medical treatment and recovery from medical illness.

Despite these obstacles, psychotherapy, pharmacotherapy, and electroconvulsive therapy for depression in the elderly can be effective and well tolerated. All antidepressant drugs are similarly effective; however, the risks and side effect profiles as well as titration requirements for the older tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs) make them more appropriate as second- and third-line agents. Due to safety concerns, these agents are best used in consultation with a psychiatrist. At least 9 newer generation antidepressants are available, and they are associated with improved safety and tolerability profiles compared with first-generation antidepressants. Among these, the medications with the largest clinical experience in the elderly are the SSRIs, which generally should be the first choice for antidepressant therapy in older patients. The efficacy of SSRIs has been demonstrated to be similar to that of the older TCAs for treating depression.[73,74] However, compared with TCAs, SSRIs have the advantage of better tolerability, with weak or absent cholinergic interactions and lack of cardiotoxicity or sedative effects.[75–80] In addition, SSRIs have a lower rate of discontinuation[77] and are less lethal in overdose than TCAs.[66,80,81] Compared with other classes of antidepressants, SSRIs have the most optimal combination of efficacy, tolerability, and lack of toxicity. Bupropion, venlafaxine, mirtazapine, nefazodone, and trazodone also show great promise, and more studies will hopefully be forthcoming regarding their use in frail and elderly patients.

Because of the physiologic differences associated with aging, physicians must keep in mind that the SSRIs fluoxetine, sertraline, paroxetine, and citalopram should be prescribed at lower doses for elderly patients than for younger patients. In particular, elderly patients may be less tolerant to therapy with fluoxetine than younger patients and may be at greater risk for extrapyramidal events,[82] apathy,[83] anorexia,[84] or inappropriate secretion of antidiuretic hormone.[85,86]

If SSRIs are not effective or tolerated, pharmacotherapy with bupropion, venlafaxine, mirtazapine, nefazodone, trazodone, or an MAOI[76,87–90] is recommended. Finally, the TCAs nortriptyline and desipramine can be used in selected patients because they have also been shown to be effective for treating depression in older patients.[91–93] However, treatment with TCAs has been associated with anticholinergic effects[79,94] and cardiac adverse effects, such as arrhythmia, increased heart rate, and slowed conduction. This may result in longer QRS, PR, and QTc intervals,[13,95,96] as well as orthostatic hypotension.[95,96] As little as 1 week of TCA therapy may also be fatal in overdose. For these reasons, TCAs should be prescribed with caution in the elderly, particularly in elderly patients with Alzheimer's disease, cardiovascular disease, or significant suicidal thoughts or ideation.

When antidepressants are effective for an elderly patient with depression, prescribing physicians also should be aware that the patient can suffer a relapse and that prevention of relapse can be accomplished by using full-dose maintenance therapy.[97–99] Stokes[98] advises that maintenance pharmacotherapy for elderly patients should be administered for 6 to 9 months past the onset of remission. The Old Age Depression Interest Group recommends a maintenance period of at least 2 years,[97] and many practitioners who treat elderly patients feel lifetime therapy is appropriate in significant late-onset depression.

When anxiety symptoms are present with depressive symptoms, as is the case in the majority of patients, older patients are often treated with hypnotics, benzodiazepines, and even major tranquilizers, which do not treat the underlying depressive syndrome. Furthermore, the increased risk of sedation and impaired cognition with these drugs places the patient at risk for falls, hip fractures, dehydration, malnutrition, aspiration pneumonia, infantilization, and further functional decline. Due to the broad affective therapeutic spectrum of activity of SSRIs in patients with comorbid depression and anxiety, pharmacotherapy with an SSRI will likely improve symptoms of both. Older patients with depression may also benefit from interpersonal psychotherapy and/or cognitive-behavioral therapy, as well as interventions aimed at increasing social supports and reducing disability and dependence. Elderly patients with low tolerability for antidepressant therapy are also candidates for psychotherapy, which may help them deal with bereavement, role transitions, interpersonal conflicts, and social isolation. It should be kept in mind that the expense associated with psychotherapy may be prohibitive, so some patients may prefer a pharmacologic approach.[2] The best approach is a combined one, and often pharmacotherapy may be the key to patients' acceptance and under-

standing of their problems, motivating them to accept psychological assistance.

Older patients with severe, chronic, or psychotic depression may be resistant to pharmacotherapy, and for some patients with depression and renal, cardiac, or hepatic impairment, medical treatment for depression may be inadvisable. For patients such as these, electroconvulsive therapy should be considered after appropriate consultation with a psychiatrist.[100–102] Physicians should be aware that post-treatment-related memory impairment or confusion might occur following electroconvulsive therapy, and, as with pharmacotherapy, maintenance therapy may be necessary to prevent relapse.[100,101,103,104]

Collaborative Care Model

Of all health care providers, primary care physicians have the greatest access to older patients with depression.[105] A strong collaborative relationship between primary and specialty providers is recommended for the treatment of depression in any setting, particularly for long-term care. Older patients with the most pressing need for referral to specialists are those who present with diagnostically complex cases, comorbid psychiatric illness, or severe medical illness, psychosis, or suicidal ideation and those who are unresponsive to an adequate trial of first-line pharmacotherapy.

SUMMARY

Depression in the elderly is a major public health problem. On its own, depression is at least as debilitating as many chronic medical diseases. Depression increases the risk for and worsens the prognosis of elderly patients recovering from stroke, MI, or hip fracture; increases the frequency and intensity of pain complaints; and contributes to malnutrition, physical decline, and poor medical outcomes. Failure to accept and comply with treatment for many medical illnesses is associated with comorbid depression. Thus, depression in the elderly is associated with a high mortality rate independent of other disease measures.

Suicide is a significant risk for older depressed patients because they have a higher rate of completed suicide than the general adult population. Screening for depression and suicidality in the primary care setting is appropriate given the frequency with which older suicide victims visit their primary caregivers for somatic complaints prior to committing suicide. Hence, primary care physicians are uniquely positioned to diagnose and treat elderly depressed patients.

In chronically ill patients with comorbid medical disease, a high index of suspicion for depression combined with an inclusive approach to making the diagnosis of depression is recommended, as antidepressant pharmacotherapy has proved to be safe and effective in this population. First-line pharmacotherapy with the newer generation antidepressants, such as the SSRIs, is preferable because of their comparable efficacy and improved safety and tolerability compared with the TCAs. Elderly patients who do not respond to antidepressant medications need liaison psychiatric consultation and may be candidates for electroconvulsive therapy. Effective therapy, including electroconvulsive therapy, should be maintained to prevent relapse in the majority of older patients. A collaborative care model in which primary and specialty providers participate in the treatment of depression in the older patient is recommended.

Drug names: bupropion (Wellbutrin), citalopram (Celexa), desipramine (Norpramin and others), fluoxetine (Prozac), mirtazapine (Remeron), nefazodone (Serzone), nortriptyline (Pamelor and others), paroxetine (Paxil), sertraline (Zoloft), trazodone (Desyrel and others), venlafaxine (Effexor).

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