Depression in the elderly
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In elderly people, depression mainly affects those with chronic medical illnesses and cognitive impairment, causes suffering, family disruption, and disability, worsens the outcomes of many medical illnesses, and increases mortality. Ageing-related and disease-related processes, including arteriosclerosis and inflammatory, endocrine, and immune changes compromise the integrity of frontostrital pathways, the amygdala, and the hippocampus, and increase vulnerability to depression. Heredity factors might also play a part. Psychosocial adversity—economic impoverishment, disability, isolation, relocation, caregiving, and bereavement—contributes to physiological changes, further increasing susceptibility to depression or triggering depression in already vulnerable elderly individuals. Treatment with antidepressants is well tolerated by elderly people and is, overall, as effective as in young adults. Evidence-based guidelines for prevention of new episodes of depression are available as are care-delivery systems that increase the likelihood of diagnosis, and improve the treatment of, late-life depression. However, in North America at least, public insurance covers these services inadequately.

Late-life depression refers to depressive syndromes defined in the American Psychiatric Association’s Diagnostic and Statistical Manual (DSM-IV) and in the International Classification of Diseases (ICD-10) that arise in adults older than age 65 years. In old age, depressive syndromes often affect people with chronic medical illnesses, cognitive impairment, or disability.\(^5\) Beyond personal suffering and family disruption, depression worsens the outcomes of many medical disorders and promotes disability.\(^6\) Although progress has been made in characterising the presentation of late-life depression and in improving its treatment, it continues to have detrimental consequences.\(^7\) Here, I offer a review of the available published work on diagnosis, pathophysiology, prevention, and management of late-life depression.

Diagnosis
For a diagnosis of major depression to be made, DSM-IV and ICD-10 state that either depressed mood or loss of interest or pleasure must be present (panel 1). Although not part of the diagnostic criteria, late-life major depression is often associated with peripheral body changes and cognitive impairment. Changes to the body include hypercortisolaemia, increased abdominal fat, decreased bone density, and increased risk for type 2 diabetes and hypertension.\(^8\) Non-demented elderly people with major depression often have difficulties with concentration, speed of mental processing, and executive function.\(^9,10\) These deficits improve, but do not completely resolve, after remission of late-life depression.\(^11\) Psychotic depression is diagnosed in patients with major depression who have a history of at least one manic or mixed episode, and bipolar disorder II is diagnosed in those who have bouts of major depression and a history of hypomanic episodes. Elderly patients with bipolar disease have severe and disabling episodes,\(^12\) increased mortality compared with their peers,\(^13\) and are high users of mental health and other medical services.\(^14,15\)

Medical comorbidity
Late-life depressive syndromes often arise in the context of medical and neurological disorders.\(^1\) The diagnosis of depression due to a general medical condition is given when depressed mood or anhedonia occur in patients already diagnosed with an illness that is associated with depression (panel 2). About a quarter of individuals who have a myocardial infarction or who are undergoing cardiac catheterisation have major depression, and another 25% have minor depression.\(^16\) Approximately half of patients with coronary heart disease and major depression will have had at least one previous episode of major depression, and 50% of those with major depression at the time of cardiac catheterisation remain depressed a year after the procedure.\(^17\) The greater the

Search strategy and selection criteria
I searched MEDLINE and Ageline abstracts to 1980 with the keywords “depression”, “depressive disorder”, “bereavement”, “geriatric aging”, “late-life”. I focused, however, on empirical studies, meta-analyses, and authoritative reviews published after 1990, since most progress in understanding late-life depression took place after this date. Among them, I selected work published in English on the diagnosis, recognition, pathophysiology, prevention, and management of late-life depression.
Panel 1: Classification and diagnosis of geriatric depressive disorders

**Major depressive disorder**

Five of the following symptoms must be present: depressed mood, diminished interest, loss of pleasure in all or almost all activities, weight loss or gain (more than 5% of bodyweight), insomnia or hypersomnia, psychomotor agitation or retardation, fatigue, feelings of worthlessness or inappropriate guilt, reduced ability to concentrate, recurrent thoughts of death or suicide. At least one of the symptoms must be either depressed mood or diminished interest or pleasure. The syndrome should last at least 2 weeks, lead to distress or functional impairment, and not be a direct effect of substance use, a medical condition, or bereavement.

**Minor depressive disorder**

At least two but fewer than five of the symptoms of major depressive disorder must be present. The syndrome should last at least 2 weeks, lead to distress or functional impairment, and not be a direct effect of substance use, a medical condition, or bereavement. This diagnosis can only be made in patients without a history of major depression, dysthymia, bipolar, or psychotic disorders.

**Dysthyemic disorder**

Sad mood for more than 2 years with no other symptoms of major depressive disorder. A duration of at least 2 years is required. An episode of major depression might not be present during the first 2 years of the disorder.

**Bipolar I disorder (most recent episode depressed)**

Individuals meet criteria for major depressive disorder and have a history of at least one manic episode or a mixed episode.

**Adjustment disorder with depressed mood**

Individuals who develop depressed mood, tearfulness, or hopelessness within 3 months of the occurrence of a stressor. The syndrome should lead to great distress or disability, and should subside within 6 months of the removal of the stressor. Bereavement is not considered a stressor for an adjustment disorder.

Panel 2: Geriatric depression syndromes associated with medical disorders and drug use

**Depression due to a general medical condition**

Patients who develop sad mood or diminished interest or pleasure in all or almost all activities and have a medical condition physiologically related to depression:

- Viral infection
- Endocrinopathy—hypothyroidism, hyperthyroidism, hypoparathyroidism, hyperparathyroidism, hypoadrenocorticism, hyperadrenocorticism, Cushing’s disease
- Malignant disease—leukaemia, lymphoma, pancreatic cancer
- Cerebrovascular disease—lacunar infarcts, stroke, vascular dementia
- Myocardial infarction
- Metabolic disorder—B12 deficiency, malnutrition

**Substance induced depression**

Patients who develop sad mood or diminished interest or pleasure in all or almost all activities within a month of substance intoxication or withdrawal or medication use causally related to the depression:

- Methylldopa
- Benzodiazeines
- Propranolol
- Reserpine
- Steroids
- Anti-Parkinsonian drugs
- β blockers
- Cimetidine
- Clonidine
- Hydralazine
- Oestrogens
- Progestosterone
- Tamoxifen
- Vinblastine
- Vincristine
- Dextropropoxyphene

Overall medical burden the higher the risk of depression. Furthermore, some postulate that stress, major depression, and medical illness are reciprocally linked—stress promotes adaptation (allostasis), but when mediators of the stress response are not inhibited (allostatic state) immunity is impaired, arteriosclerosis promoted, and obesity, bone demineralisation, and atrophy of brain cells arise. Allostatic load, expressed as increased adrenocortical activity, raised concentrations of insulin growth factor (IGF)-1, and initiation of the inflammatory response, has been documented in patients with major depression (figure). Symptoms or syndromes of depression are often present in individuals with dementia. The point prevalence of major depression is about 17% in patients with Alzheimer’s disease and is even higher in those with subcortical dementias. The US National Institute of Mental Health has developed provisional criteria for the diagnosis of depression in individuals with Alzheimer’s disease (panel 3) to help doctors to identify the problem and to promote research into the disorder. Symptoms or syndromes of depression often precede cognitive decline and dementia, with elderly individuals who have major depression and cognitive impairment likely to develop dementia within a few years of onset of depression. Depression in early life is also a possible risk factor for disorders of dementia. Major depression with onset more than 10 years before the diagnosis of dementia and lifetime history of depression is associated with increased risk for Alzheimer’s disease. Depression exacerbates the outcome of medical illnesses. In one study, elderly individuals with depression were almost four times more likely than...
those without depression to die within 4 months of a myocardial infarction. Platelet aggregation is raised in this group of patients, suggesting that depression increases the risk for cardiovascular disease. Elderly people with depressive symptomatology have poor T-cell responses to mitogens and high concentrations of plasma interleukin 6, which is indicative of inflammatory activity that might increase the risk for bone resorption. Nevertheless, late-life depression remains under-recognised and undertreated.

Psychosocial adversity

Low economic status, poor physical health, disability, social isolation, and relocation often lead to an adjustment disorder with depressed mood or trigger more severe depressive syndromes than previously present (panel 1). It is noteworthy, however, that although forced relocation has a negative effect on both morbidity and mortality, voluntary decisions to move to an institution acceptable to the individual can have a beneficial effect.

Additionally, caregivers of elderly disabled individuals are twice as likely as non-caregivers to develop symptoms of depression. This proportion might be even higher, however, since male caregivers and African-American caregivers under-report symptoms of depression. Depressive symptomatology is most likely to develop during long-term caregiving. Additional predisposing factors are a care recipient with behavioral problems and receipt of limited help from others. After placement of the elderly individual in a nursing home, a quarter of caregivers develop symptoms of depression, which remain relatively unchanged over time in women but worsen in men.

During the first year of bereavement, 10–20% of surviving spouses develop symptoms of depression, which generally persist if left untreated. Elderly individuals are less likely to become depressed than younger adults during the first months of widowhood, but rates of major depression are similar in all ages by the end of the second year. The prevalence of major depression continues to increase during the second year of bereavement, by the end of which 14% of bereaved individuals have major depression, compared with 1–4% of the elderly population in general.

Finally, some psychological traits confer vulnerability to depression (figure). Neuroticism, for example, predicted persistence of depression in primary-care patients in one study, even after severity of depression was controlled for. Furthermore, in elderly individuals with major depression, pessimistic thinking predicts suicidal ideation a year later. Elderly people who committed suicide were, however, less open to experience than both younger people who committed suicide and controls.

Late-onset depression

Late-onset major depression includes a large subgroup of patients with neurological abnormalities. Although some disagreement exists, generally, when compared with elderly individuals with early-onset major depression, individuals with late-onset major depression have a less frequent family history of mood disorders, a higher prevalence of disorders of dementia, a larger impairment in neuropsychological tests, a higher rate of dementia development on follow-up, more neurosensory hearing impairment, a greater enlargement in lateral brain ventricles, and more white-matter hyperintensities.

The study of late-onset depression has generated mechanistic hypotheses on the role of ageing-related and panel 3: Provisional diagnostic criteria for depression in patients with Alzheimer’s disease

Clinically significant depressive symptoms

Three or more depressive symptoms during the same 2-week period, representing a change from previous functioning.

At least one of the symptoms must be either depressed mood or decreased positive affect or pleasure. Other depressive symptoms are: clinically significant depressed mood—eg, depressed, sad, hopeless, discouraged, tearful; decreased positive affect or pleasure in response to social contacts and usual activities; social isolation or withdrawal; disruption in appetite; disruption in sleep; psychomotor changes—eg, agitation or retardation; irritability; fatigue or loss of energy; feelings of worthlessness, hopelessness, or excessive or inappropriate guilt; recurrent thoughts of death, suicidal ideation, plan or attempt.

Symptoms should not be a result of dementia symptoms—eg, loss of weight due to difficulties with food intake.

Depression should not be part of idiopathic depression, other mental disorders, a medical condition, or medication use.
disease-related changes in the development of depression. However, methodological and conceptual concerns limit their importance. Methodologically, onset of depression is difficult to identify, especially when mild. Conceptually, neurological changes could contribute to a late-life episode irrespective of other depressive episodes in early life (figure). Moreover, early-onset depression might be a risk factor for late-life depression by contributing to brain abnormalities that predispose to depression. One such mechanism involves stress-related hormones leading to a reduction of neurotropic factor secretion, and ultimately a decrease in neurogenesis at the dentate nucleus of the hippocampus (figure).

Depression with reversible dementia
Some elderly individuals develop dementia during episodes of depression that subsides after remission of depression (pseudodementia). Most of these patients have late-onset major depression. Furthermore, a large proportion of those with reversible dementia are left with some form of cognitive impairment after remission of depression, and about 40% develop irreversible dementia within 3 years of follow up. Thus, reversible dementia is often an early manifestation of a more permanent disorder and constitutes an indication for diagnostic work-up aimed at the identification of treatable dementia.

Depression-executive dysfunction syndrome
This syndrome has been conceptualised as major depression with prominent frontostriatal dysfunction, and is characterised by psychomotor retardation, reduced interest in activities, impaired instrumental activities of daily living, and limited insight and vegetative signs. Patients with depression and executive dysfunction often have a poor, slow, and unstable response to antidepressants and require careful treatment planning and follow-up. The depression-executive dysfunction syndrome can act as a model for studies of drugs to target neurotransmitters of frontostriatal networks, including dopamine, acetylcholine, and opioids.

Vascular depression
Cerebrovascular disease might predispose, precipitate, or perpetuate some late-life depressive syndromes. This notion is based on the comorbidity of depressive syndromes with cerebrovascular lesions and cerebrovascular risk factors and on the fact that depression often develops after a stroke. Elderly people with vascular depression have greater disability and cognitive impairment than those who are depressed but do not have vascular stigmata. Verbal fluency and object naming are the most impaired cognitive functions in patients with this form of depression. Affected individuals have more apathy, retardation, and lack of insight, and less agitation and guilt than do elderly individuals who are depressed without vascular risk factors. The vascular depression hypothesis generated hypotheses of clinical import. Drugs used for the prevention of cerebrovascular disease might, for example, reduce the risk for vascular depression. Furthermore, antidepressants that promote ischaemic recovery—eg, dopamine or norepinephrine enhancing agents—might be favoured in vascular depression and antidepressants that inhibit ischaemic recovery—eg, α adrenergic blocking agents—are best avoided.

Suicide
Suicide is almost twice as frequent in elderly individuals than in the general population. Rates of suicide in elderly individuals are raised almost exclusively in white men. Among those who attempt suicide, elderly people are most likely to die. Depressive syndromes are present in 80% of people aged older than 74 years who commit suicide. Major depression is a risk factor for suicide as is substance abuse. Minor depression, dysthymic disorder, psychotic disorders, and anxiety disorders also raise the risk of suicide. Mood disorders constitute an independent risk factor for suicide in elderly people, whereas physical illness and disability increase suicide risk, but their effect is mediated by depression. Disruption of social ties is associated with late-life suicide independently of depression, especially in individuals with a rigid, anxious, and obsessive personality. Availability of firearms doubles the risk of suicide in elderly people.

Suicidal ideation decreases with ageing, but if older people have suicidal thoughts they are at a higher risk of actually committing suicide than younger people. Suicidal ideation is closely associated with severity of depression. Findings of a study show that during an initial assessment of elderly patients with major depression, severity of depression and previous serious attempts could predict the course of suicidal ideation. During follow-up, contemporaneous severity of depression was the most important determinant of suicidal ideation over time. These observations can be used to identify elderly people with depression who are at high risk of committing suicide.

Epidemiology
1–4% of the general elderly population has major depression, equivalent to an incidence of 0·15% per year. Twice as many women as men are affected. Both the prevalence and the incidence of major depression double after age 70–85 years. Similarly, the number of elderly people with bipolar disorder is increasing, because the absolute number of old people is rising and, possibly, because the proportion of elderly individuals with this illness is increasing.

Minor depression (panel 1), has a prevalence of 4–13%. Dysthymic disorder, characterised by low-intensity symptoms of depression that last 2 years or longer, occurs in about 2% of elderly people. An elderly person is as likely or slightly less likely to have clinically significant symptoms of depression than someone who is middle-aged (prevalence 8–16%), but a very old person is...
particularly prone to this disorder. An increase in disability and cognitive impairment, a fall in socioeconomic status, and the high proportion of women who survive their partner’s death might explain this pattern.

The prevalence of late-life depressive syndromes is higher in medical settings than in the community. 10–12% of patients admitted to hospital have major depression, whereas the prevalence among primary-care patients is 6–9%. Additionally, 6% of primary-care patients have minor depression and 10% subsyndromal depression. However, more than half of patients with less severe types of depression remain depressed a year later. The prevalence of major depression among individuals who live in nursing homes is 12–14%, though 17–35% of those in long-term care have minor depression or clinically significant symptoms of depression.

Pathophysiology
Dorsal neocortical structures are hypometabolic and ventral limbic structures are hypermetabolic during depressed states. Similar changes arise in experimentally induced sadness, but are quickly reversed when stimuli are removed. The persistence of the changes in depressed patients suggests that additional biological factors predispose to depression and sustain depressive symptoms.

Frontostriatal pathways in the brain mediate positive affect-guided anticipation, and abnormalities might result in an inability to anticipate incentives, thus predisposing to depression. The left medial orbitofrontal cortex is activated in response to reward, and the right orbitofrontal cortex in response to punishment. Furthermore, the anterior cingulate gyrus has connections to brain structures, subserving functions often impaired in depression. The perigenual cingulate assesses conflicts between current function and information with motivational consequences. The dorsal cingulate monitors competing responses and modulates attention and executive functions in collaboration with the dorsolateral cortex.

Frontostriatal dysfunction could predispose to late-life depression (figure). Executive dysfunction, a clinical expression of frontostriatal abnormalities, is common in late-life depression and persists after improvement of mood-related symptoms. Additionally, subcortical disorders that compromise frontostriatal pathways are often complicated by depression and executive dysfunction. Low volumes of frontostriatal structures have been documented in late-life depression, as have hyperintensities in subcortical structures and their frontal connections. Macromolecular abnormalities in the genu and splenium of the corpus callosum, the right caudate nucleus, and the putamen are seen in elderly people with depression. Reduction in glia of the subgenual anterior cingulate and abnormalities in neurons of the dorsolateral cortex have also been observed in depressed patients.

Frontostriatal dysfunction affects the presentation and course of late-life major depression (figure), increasing executive dysfunction and psychomotor retardation and resulting in greater feelings of apathy. Executive dysfunction generally results in a slow, poor, and unstable response to antidepressants. White-matter abnormalities are associated with executive dysfunction and poor outcomes of late-life depression.

Hypometabolism of the anterior cingulate was reported in treatment-resistant major depression, while hypermetabolism arose in depressed patients with favourable treatment response. Increased left frontal error negative wave amplitude after a response-inhibition task, a function mediated by the anterior cingulate, predicts limited or slow change of major depression in elderly individuals treated with citalopram.

Abnormalities of the amygdala might predispose to depression (figure). The amygdala mediates emotions in response to aversive stimuli and signals to centres responsible for coping behaviour and autonomic activity. Age-related changes associated with attenuation of emotional perception could contribute to depressed or apathetic states. Stroke and subcortical disorders can damage the connections between the amygdala, the medial dorsal thalamic nucleus, and the orbital and medial prefrontal cortex, predisposing to depression. Additionally, hypercortisolaemia, which arises during chronic medical illnesses, is associated with increased activity of the amygdala, leading to release of cortisol and depression (figure).

During their first episode of major depression, patients have larger amygdala volumes than those with recurrent depression or healthy controls. Increased activity in this part of the brain is associated with symptoms of depression and negative emotions, and might be a result of its inadequate inhibition by prefrontal centres. Increased activity of the amygdala combined with inadequate cortical modulation of its emotional output probably contribute to depressive symptoms.

Hippocampal abnormalities could also predispose to depression (figure), since the volume of this structure is reduced during a first episode of major depression. However, some disagree with this theory. Nevertheless, a reduction in the volume of the hippocampus is correlated with lifetime duration of depression. Moreover, a decline in hippocampal volume has been documented after a first episode of major depression even in patients who received antidepressants.

Hippocampal abnormalities are relevant to the elderly population, since this structure is particularly vulnerable to aging and aging-related changes. Moreover, the CA1 hippocampal region and the subiculum are vulnerable to ischaemia and to hypercortisolaemia, resulting from stress and chronic medical illness (figure).
Heredity
In addition to changes in brain structures, hereditary factors could predispose to late-life depressive syndromes (figure). In community-residing elderly twins, heredity accounted for 18% of the variation in depressive symptoms. Elderly people who are depressed are, however, less likely to have a depressed relative than younger patients who are depressed. Personal or family history of a depressive disorder affects the incidence of depression after stroke as much, if not more, than the site of vascular lesion.

Genetic markers for late-life depression have not been identified. However, results of studies done in twins suggest an association between the serotonin 2A receptor gene promoter A/A genotype and depression in elderly men, but not in elderly women. The serotonin reuptake transporter gene was not associated with depression in elderly twins. Presence of the allele e4 of apolipoprotein-E is a risk factor for Alzheimer’s disease and for cerebrovascular disease, which are conditions associated with late-life depression. However, most investigators noted no association between e4 and late-life depression. Genes associated with increased risk for cerebrovascular lesions might increase vulnerability to depression. Patients with late-onset major depression had a higher frequency of the C677T mutation of the enzyme methylene tetrahydrofolate reductase than healthy elderly individuals. These findings suggest that genetic predisposition to late-life major depression is mediated by vascular lesions.

Prevention
There is a hypothesis that positive mental health can be enhanced if people believe they have the ability to act in a way that will result in achievement of their goals. As such, elderly individuals with chronic medical illnesses at risk for depression who receive instruction on body-mind relations, relaxation techniques, cognitive restructuring, problem solving, communication, and behavioural management of insomnia, nutrition, and exercise, have increased self-efficacy and reduced symptoms of depression, anxiety, pain, and insomnia. Other approaches to primary prevention include lowering of the risk of vascular depression—through control of hypertension, hyperlipidaemia, and concentrations of plasma homocysteine—use of antidepressants in patients at risk for depression because of medical comorbidity—eg, macular degeneration threatening complete blindness—education of elderly people about the treatment options available, and reduction of the stigma of depression to increase the number of elderly individuals who seek and adhere to treatment. The findings of secondary prevention studies indicate that antidepressants and psychotherapy alone or in combination reduce the risk for relapse and recurrence of late-life depression in elderly patients who have previously remitted. A shared-care intervention was more effective than usual care in reducing symptoms of depression in old people living in self-care units and hostels. The intervention consisted of multidisciplinary consultation and collaboration, training of family doctors and other health-care workers in detection and management of depression, and provision of education and activity programmes for residents. Finally, the results of tertiary prevention studies show that comprehensive clinical management aimed at the symptoms of depression can reduce suicidal ideation and perhaps the risk of suicide.

Management
The aims of treatment are to reduce the symptoms of depression, to prevent suicidal ideation, relapse, or recurrence of symptoms, to improve cognitive and functional status, and to help patients develop the skills needed to cope with their disability or psychosocial adversity if appropriate. Behavioural rehabilitation should be combined with antidepressant treatment to improve function as depressive syndromes subside.

Treatment planning should start with an assessment that focuses on identification of any intake of the drugs or presence of illnesses that predispose to depression (panel 2). Treatment of the underlying illness or removal of offending drugs is necessary, but is often not enough to achieve remission of depression. Antidepressants, psychotherapy, or both, are also generally needed. The combination is the preferred treatment option for late-life major depression. Pharmacotherapy or psychotherapy alone are, however, acceptable alternatives in major depression of mild severity. Electroconvulsive therapy should be considered if patients do not respond to treatment with antidepressants, have severe depression with suicide risk, are likely to die because of lack of nutrition and fluids, or are psychotic.

Antidepressants are as effective when given to elderly individuals as they are when given to younger adults. Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) are the antidepressants of choice, followed by bupropion, and mirtazapine. Although the initial doses of SSRIs and SNRIs given to elderly individuals should be low, the final doses should be similar to those used in young adults. Nortriptyline followed by desipramine are reasonable alternatives to SSRIs in severe late-life depression. Their target plasma concentrations are 60–120 μg/L and greater than 115 μg/L, respectively. Amitriptyline, imipramine, doxepin, amoxapine, maprotiline, trazodone, tranylcypromine, and isocarboxazide should be avoided.

For late-life depression initiated by a stressor, psychotherapy alone or psychotherapy combined with an antidepressant is recommended. Minor depression in late life is more likely to respond to non-specific supportive interventions than other forms of depression. Watchful waiting for at least 2 weeks is appropriate in minor depression. However, if symptoms persist for...
longer than 2–3 months, a combination of SSRI plus psychotherapy is the treatment of choice, though drug treatment alone or psychotherapy alone are reasonable alternatives.\textsuperscript{118} Cognitive-behavioural therapy, supportive psychotherapy, problem-solving therapy, and interpersonal therapy are the preferred psychotherapies for elderly people with depression.\textsuperscript{118} Cognitive therapy approaches are as effective in elderly individuals as they are in younger adults.\textsuperscript{118} Psychoeducation can help patients and their families with treatment adherence.\textsuperscript{116,127,128}

Appropriate doses of an antidepressant should be given for at least 4 weeks before the drug is judged ineffective and a different class is tried.\textsuperscript{118} If a patient’s response to an antidepressant is poor, a higher dose should be tried. If there is no further improvement, use of an augmenting agent should be considered. If the initial antidepressant was an SSRI, bupropion, lithium, or nortriptyline can be added. If the patient was initially treated with bupropion, an SSRI or lithium might help. Electroconvulsive therapy is an option at any step if the patient worsens.

In late-life psychotic depression, combinations of antidepressants (SSRIs or venlafaxine) and atypical neuroleptics (except clozapine) are recommended.\textsuperscript{118} Electroconvulsive therapy should either be considered as a first choice in psychotic depression or be used if combination drug treatment is ineffective.

Late-life depression is a recurring disorder. In one study,\textsuperscript{119} 90% of elderly individuals with major depression in remission had a recurrence within 3 years when maintained on placebo, whereas those maintained on nortriptyline and interpersonal psychotherapy had a recurrence rate of 20%, and 43% recurrent among those who received nortriptyline and medication clinic visits. For maintenance, antidepressants should be used at the same doses as for treatment. In patients who have a single severe episode of depression, antidepressant drug treatment should continue for at least 1 year. Patients with three lifetime episodes should receive maintenance treatment for longer than 3 years.\textsuperscript{118} In patients with psychotic depression who achieve remission after treatment with an antidepressant and an antipsychotic, the general recommendation is that the antipsychotic drug be continued for 6 months.\textsuperscript{118} For patients who do not respond to antidepressants but for whom electroconvulsive therapy was effective, continuation or maintenance therapy should consist of an antidepressant not yet tried by the patient and a mood stabiliser.\textsuperscript{118} Continuation or maintenance electroconvulsive therapy is another option.

**Care delivery**

Most elderly individuals who are depressed are treated in primary-care settings.\textsuperscript{120,122} However, primary-care doctors rarely diagnose depression and, when they do, often provide inappropriate treatment.\textsuperscript{120,121,129} Barriers to adequate diagnosis and treatment include doctors’ reluctance to discuss emotional problems, time constraints, and medical comorbidity, complicating diagnosis and competing for clinical attention.\textsuperscript{122,123} Perceived stigma contributes to patients’ reluctance to initiate psychiatric treatment.\textsuperscript{125,126} Furthermore, disability, cognitive impairment, and complex medication regimes undermine treatment adherence.

Several service-delivery models can improve the treatment of depression in primary care—namely, training of primary-care doctors,\textsuperscript{127} introduction of computer-driven clinical decision support,\textsuperscript{128} and integration of the management of depression with the care of other medical illnesses.\textsuperscript{129} Collaborative care, involving primary-care doctors and on-site specialists in mental health enhances quality of care and improves the outcomes of depression.\textsuperscript{128,130} Employment of depression-care managers, who use operationalised guidelines to provide on-time and on-target recommendations to primary-care doctors, and helping elderly patients with treatment adherence are more effective than usual care in decreasing depressive symptomatology and suicidal ideation\textsuperscript{131} and in leading to remission.\textsuperscript{142} However, most of these delivery models are not implemented because of inadequate insurance coverage in the USA.\textsuperscript{143}

**Outlook**

Late-life depressive disorders often arise in the context of psychosocial adversity, chronic medical diseases, and disability, and besides suffering and family disruption worsen medical outcomes. Although ageing and disease-related brain abnormalities that predispose to late-life depression have been identified, a direct lesion-depression association is unlikely. Behavioural abnormalities are subserved by high-level interactive and redundant neural systems. When damaged, these systems can cause diverse behavioural abnormalities. Personal or family history of psychiatric disorders, overall medical burden, disability, and psychosocial adversity are other factors that contribute to depression. Moreover, acquired behavioural skills could moderate or avert depressive symptoms. Finally, the patient’s own environmental ecosystem can impede or facilitate the development of symptoms and syndromes of depression, depending on whether it can compensate for the lost functions. Cognitive impairment and disability that accompany late-life depression are becoming the focus of pharmacological and non-pharmacological interventions.

The available treatments are as effective for the treatment of depression in elderly individuals as they are in younger adults. However, late-life depression is under-recognised and undertreated. Depression care-management strategies improve the outcomes of elderly individuals who are depressed and who are treated in primary-care settings. Yet, in North America at least, public insurance does not cover these services, although the cost is reasonable.\textsuperscript{144} Policy needs to catch up with science, which has made great progress’ since the 1991
National Institutes of Health Consensus Conference™ in learning how to prevent and how to treat depression in elderly individuals.

Conflict of interest statement
I have participated in scientific advisory board meetings of Forest Pharmaceuticals, and have given lectures supported by Forest, Pfizer, Lilly, Glaxo, Cephalon, Bristol Myers, and Janssen. I have received funding from Comprehensive Neuroscience to develop treatment guidelines in late-life psychiatric disorders.

Acknowledgments
This work was supported by NIH grants P30 MH68638, RO1 MH65653, and the Sanchez Foundation.

References
Seminar


