

# Depression in Older Adults

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## Key Words

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## Abstract

Depression is less prevalent among older adults than among younger adults, but it can have serious consequences. More than half of cases represent a first onset in later life. Although suicide rates in the elderly are declining, they are still higher than in younger adults and are more closely associated with depression. Depressed older adults are less likely to endorse affective symptoms and more likely to display cognitive changes, somatic symptoms, and loss of interest than are depressed younger adults. Risk factors leading to the development of late-life depression likely comprise complex interactions among genetic vulnerabilities, cognitive diathesis, age-associated neurobiological changes, and stressful events. Insomnia is an often overlooked risk factor for late-life depression. We suggest that a common pathway to depression in older adults, regardless of which predisposing risks are most prominent, may be curtailment of daily activities. Accompanying self-critical thinking may exacerbate and maintain a depressed state. Offsetting the increasing prevalence of certain risk factors in late life are age-related increases in psychological resilience. Other protective factors include higher education and socioeconomic status, engagement in valued activities, and religious or spiritual involvement. Treatments including behavioral therapy, cognitive-behavioral therapy, cognitive bibliotherapy, problem-solving therapy, brief psychodynamic therapy, and life review/reminiscence therapy are effective but are too infrequently used with older adults. Preventive interventions including education for individuals with chronic illness, behavioral activation, cognitive restructuring, problem-solving skills training, group support, and life review have also received support.

## Contents

INTRODUCTION .....	364
Life Course Perspective .....	364
EPIDEMIOLOGY .....	365
PRESENTATION .....	366
Differences from Younger Adults ...	366
Presentation in the Context of Physical and Neurological Illness .....	367
ETIOLOGY AND RISK AND PROTECTIVE FACTORS .....	368
Etiology .....	368
Genetic Risk .....	369
Biological Risk Factors and Physical Illness .....	370
Anxiety Disorder .....	373
Sleep Disturbance .....	373
Psychological Risk Factors .....	373
Social Risk Factors .....	374
Protective Factors .....	375
SUICIDE .....	377
TREATMENTS .....	378
Evidence-Based Treatments .....	378
New Treatments .....	380
PREVENTION .....	380
CONCLUSIONS .....	381

## INTRODUCTION

Because of its devastating consequences, late-life depression is an important public health problem. It is associated with increased risk of morbidity, increased risk of suicide, decreased physical, cognitive, and social functioning, and greater self-neglect, all of which are in turn associated with increased mortality (Blazer 2003). At the same time, contrary to common perception, major depression appears to be less frequent among older adults than among younger adults (Hasin et al. 2005).

Depression in older adults differs both in subtle and in obvious ways from depression earlier in the lifespan. Presentation, etiology, risk and protective factors, and potential outcomes all reflect aspects of the older adult's position in the lifespan. Knowledge of the ways in which

age may alter factors associated with the onset and maintenance of depression is essential for effective treatment of depressed older adults.

Following this introduction, we provide an overview of current research on the epidemiology, risk and protective factors, and treatment of late life depression. Wherever possible, we include information about factors that moderate risks or treatment efficacy.

## Life Course Perspective

**Age of onset of disorder.** A key distinction in discussions of mental disorder in older adults is between individuals who first experienced mental illness earlier in life and those whose first encounter with mental illness occurs in old age. The distinction portends differences in etiology and prognosis as well as differences in the lived experience of having a mental illness.

It appears that half or more of geriatric patients with major depression are experiencing a new condition arising in old age (called late-onset depression), whereas half or less have experienced their first episode of depression considerably before old age (called early-onset depression). For example, among inpatients and outpatients in a geriatric mood disorders unit, Brodaty et al. (2001) found 52% with first onset at age 60 or older, whereas 71% of depressed older home-care patients in another study were experiencing their first episode of depression (Bruce et al. 2002). However, studies of late-life depression do not systematically report proportions of cases that are early versus late onset, and the age after which onset is called "late" varies considerably. Also unknown is what proportion of those who have experienced depression earlier in life have a recurrence or continuation in later life and what proportion never again suffer a depressive episode.

There is substantial consensus that older adults with late-onset depression have distinctive risk factors and presentation. Those with early-onset depression are more likely than those with late-onset depression to have a family history of depression (e.g., Heun et al. 2001), possibly implying that the occurrence of the

disorder was genetically influenced. Those with early-onset depression may also have a higher prevalence of personality disorder or elevated scores on personality traits such as neuroticism (e.g., Brodaty et al. 2001).

The question of what leads an older adult to become depressed is most sharply raised by late-onset depression. Most scholars are now focusing their research on structural changes in the brain. Some have found that older adults with late-onset depression are more likely to have vascular risk factors (see, e.g., Hickie et al. 2001), including a history of cerebrovascular disease, although this conclusion is not always supported (e.g., Brodaty et al. 2001). Many studies—but not all—have reported that older adults with late-onset depression are more likely to have concomitant cognitive deficits, especially executive cognitive functioning deficits, or are more likely subsequently to develop dementia (see review by Schweitzer et al. 2002). Neurological findings, including white matter hyperintensities or leukoencephalopathy, are reported as common among late-onset but not among early-onset depression patients (Krishnan 2002). The particular frontal-striatal and frontal-limbic brain pathways that are disrupted by these neurological changes are involved in regulating mood. The term “vascular depression” was offered as a hypothesis to explain these findings, but it was later supplanted by the term “depression-executive dysfunction syndrome of late life” in order to encompass dysfunction that may not be exclusively caused by vascular disease (Alexopoulos 2005). As discussed at greater length later in this article, it seems likely that some proportion of late-onset depression—particularly when there is accompanying cognitive impairment or evidence of structural brain changes—represents a prodromal phase of dementia or other acquired cognitive dysfunction. As we also discuss below, a far less studied but possible explanation for late-onset depression is a response by individuals with certain long-standing vulnerabilities to the occurrence of a unique configuration of stressful life events and losses.

Of course, as pointed out by Alexopoulos (2005), even if there is a special late-onset form of depression, it may also arise in an older patient who had depression earlier in life. Thus, characteristics that define late-onset depression might be found as well in some older patients who report a previous episode of depression. For this reason, in this review we use the term “late-life depression” to encompass both early- and late-onset cases, and we only refer to age of onset where this distinction was made in the cited study.

**Lifespan developmental diathesis-stress model.** Beyond placing the onset of disorder in the life course, a lifespan perspective situates risk and protective factors developmentally, as illustrated in **Figure 1**. We discuss these factors in respective sections below. Inclusion of protective factors as well as risk factors in a developmental model is crucial to crafting an explanation for decreasing rates of depression in old age.

## EPIDEMIOLOGY

Several depressive disorders are described in the *Diagnostic and Statistical Manual for Mental Disorders* (fourth edition; DSM-IV; Am. Psychiatr. Assoc. 1994), including major depressive disorder, dysthymic disorder, bipolar disorder, and mood disorder due to a general medical condition. Adjustment disorder with depressed mood may also be considered a form of depression.

Much attention has recently been given to the experience of depressive symptoms that do not fulfill the criteria for a diagnosis of major depressive disorder. Some researchers have investigated this phenomenon using relatively well-defined categories, e.g., minor depression and subsyndromal depression, whereas other investigators have defined clinically significant depressive symptoms as a score above a threshold on a depressive symptom checklist. Some (Judd et al. 2002) but not all (Ruscio et al. 2007) evidence suggests that depression may occur on a spectrum, with symptoms that do not meet syndromal criteria for major depressive disorder

representing a less severe manifestation of the same disorder. In older adulthood, the prevalence of major depressive disorder differs from that of clinically significant depressive symptoms, as we discuss below. Nonetheless, in most cases the same risk and protective factors are associated with both. Where differences have been documented, we so indicate. In the present review, we focus primarily on major depressive disorder.

The prevalence of major depressive disorder at any given time in community samples of adults aged 65 and older ranges from 1% to 5% in most large-scale epidemiological investigations in the United States and internationally, with the majority of studies reporting prevalence in the lower end of the range (e.g., Hasin et al. 2005). Clinically significant depressive symptoms are present in approximately 15% of community-dwelling older adults (Blazer 2003). Rates of depression appear to be higher in older women than in older men, but with the gender gap somewhat narrower in this age group, particularly among the oldest old, than the twofold difference seen across the rest of the adult lifespan (Djernes 2006). Few differences exist in depression prevalence by race or ethnicity, although depressive symptoms may be more common among Hispanic older women than among non-Hispanic whites (Swenson et al. 2000).

Rates of major depression among older adults are substantially higher in particular subsets of the older adult population, including medical outpatients (5%–10%, though estimates vary widely), medical inpatients (10%–15%), hospice and palliative care patients (10%–25%, though based on sparse research), and residents of long-term care facilities (14%–42%; Blazer 2003, Djernes 2006, King et al. 2005). Congregate living arrangements are not depressogenic per se, as shown by the lower rate of depression found among older kibbutz residents compared to community samples (Blumstein et al. 2004); rather, relocation to congregate living is typically occasioned by health issues and/or loss of a caregiving spouse.

Prevalence rates of major depression in community samples of older adults reflect a significant decline from midlife prevalence rates for both men and women. In contrast, most studies that measure elevated scores on a depressive symptom checklist (rather than diagnosis of a depressive disorder) report higher rates of clinically significant depressive symptoms among older adults than among those in midlife (Newmann 1989). How should these differences in prevalence be interpreted? The diagnostic rubric for major depressive disorder may underestimate the disorder among older adults. Current diagnostic criteria privilege dysphoria, a symptom less frequently endorsed by older adults compared to younger adults (Gallo et al. 1994), and require a judgment that symptoms are not attributable to the direct physiological effects of a medication or general medical condition or to a recent bereavement. Conversely, depressive symptom checklists are inflated because they include symptoms that are directly linked to a physical illness or bereavement, both of which increase in frequency with age. As Blazer (2003) and others have demonstrated, depressive symptoms actually decrease in frequency with age after accounting for the effects of gender, education, physical illness, and bereavement, though it should be noted that physical illness and bereavement can be causes of depression rather than simply confounds. Thus, the preponderance of evidence indicates that depression becomes less common and less severe with age but that lower-severity depressive symptoms, which can also be consequential and treatable (Judd et al. 2002), should not be overlooked. We elaborate reasons for age differences in depressive symptom prevalence below; first we turn to age differences in presentation of depression.

## PRESENTATION

### Differences from Younger Adults

Depression in older adults may present somewhat differently from depression in younger adults. For example, older adults are less likely

to endorse cognitive-affective symptoms of depression, including dysphoria and worthlessness/guilt, than are younger adults (Gallo et al. 1994). Sleep disturbance, fatigue, psychomotor retardation, loss of interest in living, and hopelessness about the future may be more prevalent in late-life depression than in depression in younger or middle-aged adults (Christensen et al. 1999). Subjective complaints of poor memory and concentration are also common among depressed older adults. Slower cognitive processing speed and executive dysfunction are frequent findings from objective testing (Butters et al. 2004). Overall, there do not appear to be substantial differences by gender or ethnicity. Some evidence suggests that older African Americans are even less likely to report dysphoria than are European-Americans and more likely to report thoughts of death (Gallo et al. 1998). With respect to somatic symptoms, depressed older women report more appetite disturbance than do men, whereas older men report more agitation (Kockler & Heun 2002).

Several geriatric-specific variants of depression have been proposed. One variant, reflecting the predominant age differences in presentation, has been called “depression without sadness” or “depletion syndrome” (Gallo et al. 1997, Newman et al. 1991). Another variant is the depression-executive dysfunction syndrome (Alexopoulos 2005). As the name indicates, cognitive performance in this syndrome is typically impaired on measures of verbal fluency, naming, and initiation/perseveration. The syndrome also includes psychomotor retardation and anhedonia, but vegetative symptoms, agitation, and guilt are less severe than in other types of depression.

Two other largely geriatric variants, depression of Alzheimer disease and depression in Parkinson’s disease, are discussed below.

### **Presentation in the Context of Physical and Neurological Illness**

As noted, depression rates are markedly elevated in those with other medical conditions. However, measurement issues may confound

the issue of comorbidity. According to the DSM-IV, major depressive disorder cannot be diagnosed when symptoms are the direct physiological result of a medical condition. Thus, depression may be either underdiagnosed or overdiagnosed in the presence of conditions such as cancer that can cause fatigue and weight loss. Overattributing these symptoms to the physical illness even when other mood symptoms are present represents underdiagnosis. Failing to take the physical illness into account can lead to overdiagnosis. Among patients at the end of life, diagnosis also entails differentiating depression from the expectable, nonpathological reaction to terminal illness. The treatment of depression among the terminally ill is important, as untreated depression can reduce the quality of a patient’s limited remaining time.

Depression presents differently among patients with neurological syndromes. Depression following stroke, especially stroke with right hemisphere damage, is less likely to include dysphoria and is more strongly characterized by vegetative symptoms than are other forms of late-life depression (Paradiso et al. 2008). Depression associated with Parkinson’s disease (PD) is a milder form of depression and is associated with dysphoria and anhedonia less frequently than is depression in older adults without neurological illness (Ehrt et al. 2006). In order to avoid underdiagnosing depression in PD, a study group that proposed the specific syndrome, depression in Parkinson’s disease, recommends an inclusive approach in which all symptoms are “counted” toward a diagnosis of major depression even if they overlap with PD symptoms (Marsh et al. 2006).

Diagnosing depression in the context of dementia is complicated by deficits in verbal expression and potential confounding with cognitive symptoms, which has led to the development of diagnostic criteria to describe comorbid Alzheimer disease (AD) and depression (see Olin et al. 2002). Depression of Alzheimer disease is diagnosed in the presence of three or more symptoms of major depression, not including difficulty concentrating, but including additional nonsomatic symptoms

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**PD:** Parkinson’s disease

**AD:** Alzheimer disease

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such as irritability and social withdrawal. Depression comorbid with vascular dementia, compared to depression comorbid with AD, is characterized by more vegetative symptoms such as fatigue, muscular weakness, and weight loss (Park et al. 2007).

## ETIOLOGY AND RISK AND PROTECTIVE FACTORS

### Etiology

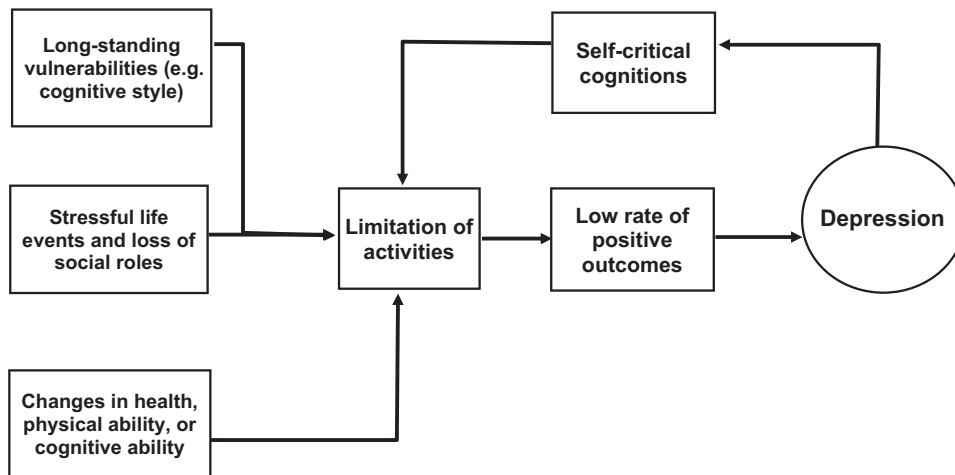
Why might a person become depressed, especially for the first time, in old age? **Figure 1** provides a lifespan view of risk factors that may help to explain the occurrence of depression in an older person. Biological factors loom large in late life. Both cardiovascular and neurological changes that occur with normal aging or with age-associated diseases appear to increase vulnerability to depression. But these explanations are not sufficient in light of the fact that neurobiological changes are ubiquitous with aging and physical disease is not uncommon, yet only a small fraction of older adults become depressed. It would also be easy to point to all of the losses that characterize later life; yet most older adults experience stressful life events and only a small proportion become depressed. For these reasons, we suggest that the onset and maintenance of depression in late life can be understood as an interaction between certain vulnerabilities, including genetic factors, cognitive diathesis and age-associated neurobiological changes, and the types of stressful events that occur with greater frequency in late life than earlier in the lifespan.

Behavioral explanations of depression that are not specific to late-life disorder focus on a relative lack of events with positive outcomes (Lewinsohn et al. 1986). Because engagement in activities is not reinforced, frequency declines, resulting in turn in fewer opportunities for interactions with the environment that have positive outcomes. Compared to nondepressed individuals, those who are depressed exhibit social skill deficits that are likely to lead to less engagement and more negative outcomes.

Although not emphasized in Lewinsohn et al. (1986), self-critical cognitions may also play a role in curtailing a depressed person's engagement in activities. In the depressed person, activities are often followed by self-critical cognitions, which would have a punishing effect on the person's efforts, resulting in a further decline in the engagement in activities. Because the self-critical internal verbalizations also function to provide a rationale for not engaging in future behaviors that are deemed likely to result in failure, the cognition may be negatively reinforced and thus more likely to occur in the future. The result would be a feedback loop in which negative cognitions reduce the level of active engagement with the environment, and the cognitions are maintained by the relief associated with not risking additional failure. Thus, both the lack of opportunity for positive outcomes and the aversive experience of self-critical cognitions may intensify and maintain a depressive state. **Figure 2** illustrates this model.

Aging is replete with reasons to reduce activity or even engage in occasional negative self-talk, but certain individuals may be more likely than others to do so when faced with the particular types of stressful events that are most common in late life. For example, stressful events that involve threats to competence (e.g., functional and cognitive limitations), which become predominant in late life, may pose special risks for people who more heavily value personal success and control. Role changes associated with spousal bereavement, e.g., taking on tasks such as household management, driving, and social planning that were formerly performed by the spouse, may lead to a reduction of activities and an increase in negative self-evaluation, particularly among older adults who are less flexible or less open to experience. Finally, pervasive negative stereotypes about aging may increase the likelihood that older adults, especially those with a neurotic style, would engage in self-critical thoughts.

In summary, many of the changes that accompany aging could lead to reduced engagement with the environment, particularly



**Figure 2**

Behavioral model depicting onset and maintenance of depression in late life.

among individuals with existing vulnerabilities; if this process is not interrupted (e.g., through encouragement or support for taking on new, meaningful activities and roles), the outcome is likely to be a depressed mood, maintained and intensified by concomitant self-critical cognitions.

The process described in this model has implications for intervention. In addition to behavioral activation and cognitive restructuring, which have substantial evidence as effective treatments for late-life depression (reviewed below), interventions that emphasize acceptance rather than personal control, increase flexibility of responses, and combat stereotypes about aging may be effective for certain depressed older adults who present with these vulnerabilities.

In the following sections, we review in more detail factors that are associated with increased risk of depression in late life, including genetic risk, nongenetic biological factors and physical illnesses, anxiety, sleep disturbance, psychological risk factors, and social risk factors, as well as protective factors shown to buffer those risks. We caution that some evidence is cross-sectional and therefore can only definitively demonstrate that a given factor is a correlate; we indicate in the text where conclusions

are based on longitudinal research. Where supported empirically, we include information on factors that moderate the effects of risk and protective factors.

### Genetic Risk

Genetic risk seems to express itself most strongly earlier in the lifespan rather than later. Kendler and colleagues used data from a telephone interview with all members of the Swedish Twin Registry to estimate heritability of major depression in twins aged 42 and older (average age at assessment = 56). Heritability was 42% for females and 29% for males, with no difference by birth cohort (Kendler et al. 2006a). Risk of major depression in the cotwin was higher when age of onset was earlier in the depressed twin, with first onset older than age 35 not meaningfully affecting risk of depression for the cotwin (Kendler et al. 2005).

The search for specific genes associated with depression in older adults has encompassed both genes studied in the nongeriatric population and genes that might relate to distinctive aspects of late-life depression. Genetic studies in the nongeriatric population have for the most part focused on the short variant of an insertion/deletion polymorphism located in the

promoter region of the serotonin transporter gene (5-HTTLPR). In one of the few extensions of this work to older adults, Jansson and colleagues (2003) found a significant effect for the A/A genotype of the 5-HTR2A gene promoter polymorphism and depressed mood for older males but not for older females. In this study, the 5-HTT serotonin transporter gene was not associated with depressed mood.

Interest in identifying genes that might account specifically for late-life depression has centered on genes known to be associated with vascular risks, including the  $\epsilon 4$  allele of apolipoprotein E (APOE4), which influences lipid metabolism; the insertion/deletion polymorphism of the gene encoding for the angiotensin converter enzyme dipeptidyl carboxypeptidase-1 (DCP-1); the five-repeat polymorphism of the gene encoding for very-low-density lipoprotein-receptor (VLDL-R); and the C677T gene mutation of the methylenetetrahydrofolate reductase enzyme (MTHFR), which may lead to raised plasma homocysteine levels. Of these genes, the most studied is APOE4, an established genetic risk factor for Alzheimer disease. Despite the plausibility of the association and one report of increased APOE4 frequency in older depressed patients (Krishnan et al. 1996), most subsequent studies have found APOE status to be unrelated to depression in older adults (e.g., Cervilla et al. 2004, Hickie et al. 2001, Hwang et al. 2006). Some found depressed APOE4 carriers to have poorer cognitive performance than depressed noncarriers (Hwang et al. 2006, Krishnan et al. 1996), while others found APOE4 unrelated to level of cognitive functioning in depressed older adults (e.g., Hickie et al. 2001). There have been inconsistent findings as to whether having the  $\epsilon 4$  allele is related to age of first onset of depression (Krishnan et al. 1996, Hickie et al. 2001, Hwang et al. 2006). Finally, one study reported that APOE4 in depressed older adults was related to history of suicide attempts (Hwang et al. 2006).

With respect to other polymorphisms related to vascular disease, Hickie et al. (2001) found that the MTHFR mutation did not differ

between depressed and nondepressed individuals, but that it was significantly more common among late-onset (age of onset 50 and older) than early-onset (onset before age 50) depression cases. Cervilla et al. (2004) reported that neither VLDL-R nor DCP-1 was associated with late-life depression. No analyses by age of onset were presented.

## Biological Risk Factors and Physical Illness

Nongenetic biological risk factors for depression are particularly important in old age, largely because of age-related changes that make them more common in older adults. These biological risks include endocrine, inflammatory or immune, cardiovascular, and neuroanatomical factors. Furthermore, biological status may interact with efficacy of treatment.

It is well established that late-life depression frequently occurs in the context of medical illness. Although virtually any serious or chronic condition can produce a depressive reaction, the conditions believed to be most strongly associated with depression include cardiac and cerebrovascular disease and neurological conditions, discussed in more detail below. Depression may also be caused by infections or malignancies. Diabetes has been investigated as a risk factor for depression, although recent research suggests that depression may actually be a risk factor for the development of diabetes.

Depression rates are elevated in hyper- as well as hypothyroidism, suggesting that endocrine dysregulation may cause late-life depression (Tiemeier 2003). Allostatic load, a construct that includes a number of biological variables such as increased adrenocortical activity, elevated insulin growth factor-1, and inflammatory markers, is associated both with accelerated aging on the cellular level and with depression in later life (Alexopoulos 2005). Late-life depression is also associated with bone loss; this may be due to the role of inflammatory markers in both conditions (Alexopoulos 2005).

Depression may be caused by certain medications (such as beta blockers, central nervous system medications, calcium channel blockers, digitalis, corticosteroids, hormones, anti-Parkinson agents, respiratory or gastrointestinal medications, certain cancer medications, benzodiazepines, and interferon) (Alexopoulos 2005, Djernes 2006). Diastolic hypotension is associated with low positive affect, which may explain why depression can be a side effect of certain antihypertensive drugs such as beta blockers (Blazer 2003).

It is important to note that biological risk factors may interact with psychosocial factors as well as depression itself. Depression in medically ill patients often leads to higher levels of morbidity and disability, although evidence for elevated mortality risk associated with depression is mixed (Charlson & Peterson 2002). For many physical disorders, experiences related to the disorder, such as the demands of managing a chronic disease, functional limitations or pain due to the disease, and vision or hearing loss, can provoke a depressive reaction (Djernes 2006, Vink et al. 2008). In turn, depression makes treating the disease more difficult. For example, appetite disturbance secondary to depression is a major cause of weight loss in the elderly, and weight loss is associated with frailty and failure to thrive (Blazer 2003). Loss of appetite can also lead to compromised nutritional status, and some evidence suggests that nutritional deficiencies may play a role in the development of depression. Low levels of vitamin B12 and the ratio of omega-6 to omega-3 fatty acids appear to be associated with late-life depression even after controlling for other risk factors (Tiemeier 2003).

Not all neurobiological risks have later-life origins. For example, depression earlier in life may predispose an individual to late-life depression through stress-related hormones leading to reduced secretion of neurotropic factors and decreased neurogenesis (Alexopoulos 2005). Furthermore, depression earlier in life may be a risk factor for vascular disease, which in turn can increase risk of late-life depression. This association suggests that these

two disorders may share a common pathological process (Tiemeier 2003). For example, the serotonin transporter promoter polymorphism 5-HTTLPR associated with depression is also associated with higher platelet factor 4 and beta-thromboglobulin levels, leading to increased platelet activation (Alexopoulos 2005, Blazer 2003).

**Cardiovascular disease.** Depression is particularly prevalent in cardiovascular disease. Approximately 20%–25% of heart disease patients experience major depression, and another 20%–25% report symptoms of depression that do not meet criteria for major depressive disorder (Carney & Freedland 2003). Consequences of depression in heart disease patients include rehospitalization, slower recovery, disability, mortality, and increased health care costs (Krishnan et al. 2002).

Several mechanisms have been proposed for the link between heart disease and depression, including poor adherence to treatment and lifestyle recommendations; shared genetic influences as described above; dysfunction in the sympathetic, neuroendocrine, autonomic, immune, and inflammatory systems; increased platelet activity; and cerebrovascular disease (Krishnan et al. 2002). One recent large-scale study among patients with coronary heart disease found evidence for genetic influences and poor adherence to medications but no evidence for a link between depression and inflammatory processes (Gehi et al. 2005, Otte et al. 2007, Whooley et al. 2007).

**Diabetes.** Prevalence estimates for depression in patients with type II diabetes are as high as 15% for major depression and approximately 20% for elevated depressive symptoms (Li et al. 2008). Although conventional wisdom holds that diabetes causes depression, studies have reached discrepant conclusions as to whether impaired glucose metabolism is a risk or a protective factor for depression (Golden et al. 2008, Maraldi et al. 2007). Recent prospective research strongly suggests that risk of diabetes is higher in patients with major depressive

disorder or elevated depressive symptoms and appears to be independent of health behaviors and other risk factors (Engum 2007, Golden et al. 2008). Overall, contrary to what is commonly reported, the evidence appears to be stronger for depression as a risk factor for diabetes than the reverse.

**Dementia.** There is substantial comorbidity of major depression and dementia, and differential diagnosis is often challenging. Major depression with cognitive impairment was once considered a form of reversible dementia. In fact, cognitive impairment in conjunction with major depression may not completely reverse as the depression abates (e.g., Butters et al. 2000), and individuals who have late-onset major depression with cognitive impairment are especially at risk of developing AD, with as many as 40% developing dementia within three to five years (Alexopoulos 2005, Schweitzer et al. 2002).

Still controversial is whether depression prior to dementia represents a risk factor for dementia or a prodromal feature of dementia (see meta-analyses by Jorm 2001 and Ownby et al. 2006). What seems most likely is that depression can be both an early or midlife risk factor for dementia and an early sign of incipient dementia, with both dementia and depression resulting from the same neuropathological changes. Most studies find that the risk of subsequently developing dementia is greater when there is a shorter interval between the diagnoses of depression and AD (e.g., Green et al. 2003). In another recent report, Geda and colleagues (2006) followed a cohort free of both depression and cognitive impairment. Those who developed depression were more likely subsequently to develop mild cognitive impairment or incident dementia, with the effect stronger for those who did not have a previous history of depression.

Finally, dementia may be a risk factor for depression due to psychological reaction to the cognitive and behavioral changes accompanying dementia. Because depression adds an additional burden to quality of life in demented

patients (and their caregivers), it is important to treat.

**Other neurological disorders.** Rates of major depression are highest among stroke patients (20%–25%; Park et al. 2007) and intermediate among those with PD (15%–20%; Reijnders et al. 2008), compared to 10%–15% among those with AD (Park et al. 2007). Comorbid depression is associated with functional impairment (e.g., Goodwin & Devanand 2008). For example, in PD, depressive symptoms increase motor disturbance (Ravina et al. 2007). In addition to evidence indicating that depression often develops in the course of neurological illness, depressive symptoms appear to be a risk factor for incident stroke (Wouts et al. 2008) and PD (Ishihara & Brayne 2006).

Much attention has been paid to neuroanatomical and chemical changes in the central nervous system as risk factors for depression and as predictors of poor response to treatment. Frontal, basal ganglia, and subcortical white matter lesions may be responsible for the phenomenon of depression-executive dysfunction syndrome (Alexopoulos 2005, Krishnan 2002). Structural abnormalities in various brain regions have been observed in depressed older adults (Alexopoulos 2005, Blazer 2003). Functionally, depression is associated with hypoactivity in cortical structures and hyperactivity in limbic structures, and hypometabolism of the anterior cingulate is associated with treatment resistance (Alexopoulos 2005). Reduced connectivity between the amygdala and structures in the thalamus and frontal cortex that regulate emotional processing may contribute to the maintenance of late-life depression (Alexopoulos 2005). Studies have found a reduction in glial cells and neuronal abnormalities associated with late-life depression, suggesting possible mechanisms for this decreased connectivity.

In summary, vascular, neuroanatomic, and inflammatory risk factors are associated with depression. These different classes of biological risk factors may furthermore be associated with distinct symptom profiles. Naarding

et al. (2005) found vascular risk factors were associated with sleep disturbance, psychomotor change, and loss of energy; neuroanatomic risk factors were associated with psychomotor change and concentration disturbance; and inflammatory risk factors were associated with appetite and sleep disturbance, loss of energy, concentration disturbance, and thoughts of death. Minor depression appears more closely related to inflammatory risk factors than to vascular or degenerative changes.

## Anxiety Disorder

As in younger adults, anxiety typically precedes depression in older adults (Wetherell et al. 2001), suggesting that anxiety disorders may be a risk factor for late-life depression (Hettema et al. 2006). Estimates of the prevalence of anxiety disorders in older adults with depression are as high as 50% (Beekman et al. 2000, Lenze et al. 2000). Prevalence estimates of depression in older adults with anxiety disorders range from 25% to more than 80% (Beekman et al. 2000, Schoevers et al. 2003).

Late-life depression is more severe, persistent, and difficult to treat when combined with anxiety (e.g., Andreescu et al. 2007, Schoevers et al. 2003). Rates of somatic symptoms, disability, and suicide are higher in older adults with anxiety superimposed upon depression than in those with depression alone (Jeste et al. 2006, Schoevers et al. 2003). Anxiety may also increase the risk of cognitive decline among older adults with treated depression (DeLuca et al. 2005). The impact of treating anxiety prior to or concurrent with treatment of depression has not been investigated.

## Sleep Disturbance

Sleep disturbance is a risk factor for depression among older adults, with a pooled odds ratio of 2.6 and a population-attributable risk of 57.0% demonstrated in a meta-analysis (Cole & Dendukuri 2003). Insomnia, a type of sleep disturbance, becomes more common with age, affecting 25% of older men and as many as 40%

of women in their 80s (Lichstein et al. 2006). Prospective studies have recently shown that insomnia, which was previously conceptualized as a symptom of depression, often precedes the onset of depression (Perlis et al. 2006). Among older adults, insomnia is a risk factor for both onset and persistence of depression. Acute insomnia may be conditioned or may be maintained by a person's compensatory behaviors, such that it takes on a chronic course independent of the original precipitating factors. Residual insomnia symptoms often persist after remission of a depressive episode and predict earlier relapse. Promising recent research in a mixed age sample shows that concurrent treatment for comorbid insomnia may enhance effects of depression treatment (Manber et al. 2008).

## Psychological Risk Factors

Psychological factors that increase the risk of depression in late life include many of the same characteristics that are related to depression earlier in the lifespan (Nolen-Hoeksema & Ahrens 2002). High scores on personality scales measuring neuroticism are strongly related to depression in late life. A large part of the relation between neuroticism and depression in middle-aged and older adults has been shown to be a function of shared genetic vulnerability, suggesting that neuroticism can be viewed as an index of genetic risk for depression as well as a psychological risk (Kendler et al. 2006b).

Both rumination and avoidance are associated with depression across the lifespan. Rumination is an ineffective coping style that involves repeatedly but passively thinking about one's distress. In older adults as well, a ruminative coping style has been associated with depression (Garnefski & Kraaij 2006). Individuals who endorse a ruminative style benefit more from social support but report receiving less of it than people who report that they ruminate less (Nolen-Hoeksema & Davis 1999), presumably because the social support network may be overtaxed.

An avoidant coping style, which has largely been studied with respect to anxiety, has recently been implicated in depression. In an older adult sample, the effect of poor health on depression was stronger among those with higher scores on a measure of experiential avoidance (Andrew & Dulin 2007).

### Social Risk Factors

Social risks such as stressful life events and inadequate social or practical support do not figure as prominently in old age as earlier in the lifespan, although they may increase again in importance in very old age, when individuals are faced with greater losses in the context of fewer resources. Social disadvantage early in life can also have cumulative effects that have renewed importance in later life.

**Stressful life events.** The number of stressful life events a person experiences has been associated with depression in late life, as at other ages (Nolen-Hoeksema & Ahrens 2002), although the relative frequency of different types of events may change with age. Stressful events in late life include such factors as financial difficulties, bereavement, a new physical illness or disability in self or family member, change in living situation, and interpersonal conflict. Retirement is not associated with depression in most older adults, although men who retire early may experience an elevated risk for reasons that remain to be explored (Butterworth et al. 2006). Studies examining recent events suggest that the greatest impact occurs within six months of a stressful life event, suggesting that most individuals are fairly resilient. Nevertheless, even long-past events contribute to risk.

Long-standing vulnerabilities appear to modify the effects of stressful events on depression in older adults. For example, a variant of the serotonin transporter gene promoter region (s allele of the 5-HTTLPR) is associated with increased risk of depression following hip fracture (Lenze et al. 2005). Cognitive style also influences a person's response to stressful events,

and the response appears to vary based on the interaction between cognitive style and type of event. Among older adults with higher scores on a measure of sociotropy (need for close relationships, interpersonal dependency, and a concern about approval), stressful events of an interpersonal nature were most closely associated with depression, whereas among older adults with high scores on an autonomy scale (emphasis on personal control and success), negative events associated with achievement (e.g., loss of long-term residence) were more strongly associated with depression (Mazure et al. 2002).

A reciprocal relation between stressful life events and depressive symptoms in older adults has also been demonstrated (Fiske et al. 2003), consistent with the notion that individuals who are depressed behave in ways that increase the likelihood of future stressful events. Although not yet tested, it is conceivable that depressed older adults may be particularly likely to create future problems of an interpersonal nature for themselves (e.g., alienating caregivers), as has been observed among younger depressed individuals (Hammen 1991). Rumination, which has been linked to decreased social support, may play a role in this process.

A stressful event that occurs with greater frequency as one grows older is bereavement. Depressive symptoms are an expected reaction to loss, but pervasive symptoms lasting more than two months may signify a depressive disorder. Some have proposed that depression associated with bereavement is a distinct syndrome called complicated grief and characterized by symptoms of separation distress and traumatic distress (Prigerson et al. 1995). Others have argued, however, that the similarities between complicated grief and standard major depression outweigh the differences (Zisook & Kendler 2007).

A meta-analysis of prospective studies of depressive symptoms and disorders in adults aged 50 or older found that bereavement more than tripled the risk of depression, with the largest effect size of any risk factors examined (Cole & Dendukuri 2003). Even so, bereavement confers less risk of depression for older adults than

for middle-aged adults. Older adults are more likely than younger adults to resolve regrets associated with the loss, and such resolution has been linked to better adaptation after the loss (Torges et al. 2008). Compared to women, men are more likely to become depressed following loss of a spouse and to remain depressed longer. This outcome may be due to the fact that the loss of a spouse involves different strains for men and women, reflecting their different roles in the marriage: for widowed women, financial strain is the primary mediator of depressive symptoms, whereas for men, the mediator is primarily household management (Umberson et al. 1992).

Providing care for an ill or disabled relative also represents a stressor that is more frequent in late life and may place some individuals at risk for depression. Although high rates of depression among caregivers have been reported, estimates vary widely, and elevated rates are largely based on help-seeking samples. A recent population-based study found no differences in depression between caregivers and noncaregivers matched for ethnicity, gender, and age (Knight et al. 2007). Aspects of the care recipient's illness are related to depression in the caregiver. Greater risk of depression is found among individuals caring for a person with dementia than among those caring for a person with a physical disability, and greater severity of behavior problems and distress in the care recipient also predict depression in the caregiver (Schulz et al. 2008). Some evidence suggests that the relation between severity of the care recipient's illness and depression in the caregiver may be explained by restriction of the caregiver's normal activities (Williamson & Shaffer 2000).

**Problems with social support.** Deficits in social support, negative aspects of the social network, and even excessive amounts of support have been studied as risk factors for depression in late life, but discerning whether they are the cause or effect of depression can be problematic. In particular, troubled relationships, including marital conflict, perceived fam-

ily criticism, and depression in the spouse, may be a factor in explaining late-life depression (Nolen-Hoeksema & Ahrens 2002). Although older adults are less lonely than their younger or middle-aged counterparts, loneliness is associated with depression in this age group (Nolen-Hoeksema & Ahrens 2002). Social support that is perceived as excessive or unhelpful may be a risk factor for depression. Increased levels of depressive symptoms associated with the receipt of social support have been found among older men with physical limitations who endorsed a greater desire for independence (Nagurney et al. 2004). Thus, it appears that the quality, not the quantity, of social support is important in the development of depression, and the effects of these social variables may vary based on factors associated with both the person and the context.

**Socioeconomic factors.** Socioeconomic factors play an important role in late-life depression. Deterioration in financial status is among the most frequently endorsed stressful life events experienced by older adults (Fiske et al. 2003). Older adults who are economically disadvantaged are more likely to experience persistent depressive symptoms (Mojtabai & Olfson 2004), consistent with the chronic nature of the stressors associated with low income, including financial strain and exposure to unsafe and unstable environments. Practical issues such as these may also complicate treatment for those low-income older adults who are depressed (Areán et al. 2005). In addition, socioeconomic disadvantage early in life may increase vulnerability to depression throughout the lifespan through the effects of poor nutrition, reduced opportunities for education, less access to health care, or other mechanisms. The effects of early disadvantage may become even more consequential with age, as economic and health disparities are compounded.

## Protective Factors

Since most older adults experience disability, bereavement, or other stressful events in late

life, and since most older adults have age-related changes in immune, neurological, and other biological systems, it is of considerable interest to know why most older adults do not experience depression. Of special interest would be to study individuals with early-onset depression that did not persist into late life. There is, however, extensive research on psychological and social factors that appear to buffer against depression or depressive symptoms in the context of stressful events and biological risks (see review by Hendrie et al. 2006). Three themes emerge: (a) the importance of resources—health, cognitive function, socioeconomic status; (b) the idea that the life experiences of older adults have taught them psychological strategies and ways to use social support to manage their health-related stresses; and (c) the role of meaningful engagement, whether in social activities, volunteer work, or religion.

Improvements in emotion regulation with age appear to play an important role in protecting against depression in older adults. Experiencing negative affect declines with age, with the lowest scores seen in older adults (Charles et al. 2001). Older adults are less reactive to stressors, particularly those of an interpersonal nature, than are younger adults (Neupert et al. 2007). When compared to younger adults with the same number of chronic health conditions, older adults endorsed less negative affect and demonstrated less reactivity to daily stressors (with the exception that older adults with the greatest number of illnesses displayed the same level of reactivity as younger adults; Piazza et al. 2007). Similarly, older adults experienced less affective reactivity in response to a cognitive challenge task than did younger adults (Chow et al. 2007).

Older adults are as likely as younger and middle-aged adults to report engaging in the cognitive strategy of positive reappraisal, which is associated with decreased depressive symptoms across age groups, and more likely to report putting into perspective, a cognitive strategy linked to lower depressive symptom scores only in the elderly (Garnefski & Kraaij 2006). Older adults have been shown to focus more

on positive and emotionally meaningful experiences than do younger adults, which also suggests better emotion regulation with aging (Carstensen et al. 2003).

Other psychological factors associated with resiliency in late life include a positive self-concept, a sense of mastery, or self-efficacy. Although these factors are often conceptualized as moderators, in a longitudinal analysis, sense of control and self-esteem were found to mediate the relation between functional disability and depressive symptoms. That is, disability was associated with decreases in mastery and self-efficacy, which were associated with increases in depressive symptom scores. The effects were large, accounting for 53% of the effect of baseline functional disability on depressive symptoms and 43% of the effect of change in disability on change in depressive symptoms (Yang 2006). Disability may lead directly to a reduction in a person's appraised ability to achieve goals, but it is also possible that individuals reduce their activities when disability makes it difficult to continue them, and the lack of regular engagement in activities leads to decrements in skills and associated lack of self-efficacy.

Whereas activity restriction is associated with increased levels of depression among older adults with functional impairment (Williamson & Shaffer 2000), replacement of lost activities can lead to a normalization of depressive symptoms, but only satisfactory replacement activities have this effect (Benyamini & Lomranz 2004). Whether proactive efforts to replace lost activities can protect against the onset of a depressive episode remains to be examined.

The preponderance of evidence indicates that perceived social support buffers the effect of stressful events in older adults. One way in which social support may help is through encouraging a person to engage in meaningful activities. As discussed above, delivery of social support must be tailored to the individual or may inadvertently lead to negative effects.

Religious involvement, which is more frequently endorsed by older adults than by other age groups, may also reduce the risk of depression in this age group (George et al. 2002).

Effects are not entirely explained by social factors and may reflect an increased sense of meaning in one's life or other variables yet to be fully examined.

Factors thought to buffer the effects of biological vulnerability to depression in late life have received less attention, but some recent work has examined physical exercise, stress-reduction strategies, and hormone replacement therapy. Engaging in active behaviors to overcome health problems, referred to as health-engagement control strategies, is associated not only with reduced levels of depressive symptoms, but also with reduced secretion of the stress hormone cortisol (Wrosch et al. 2007). Efforts to promote vascular health may also protect against late-life depression associated with vascular risk factors, though prevention trials would be required to examine this question.

## SUICIDE

A particularly tragic potential outcome of depression in late life is suicide. Although research in mixed-age samples indicates that only 4% of individuals with an inpatient admission for depression will die by suicide (Bostwick & Pankratz 2000), most people who do die by suicide were depressed. Furthermore, suicide among older adults is more likely to be associated with depression than suicide at any other age (Conwell & Brent 1996). This fact is particularly troubling because depression can be effectively treated in late life (as we discuss below).

Suicide rates in most countries and cultures are three to four times higher among men than women at all ages, but the differential increases in late life compared to midlife due to a dramatic increase in risk for men and a slight decrease for women (Kung et al. 2008). Suicide rates vary by ethnicity, with the highest risk in the United States for whites and Native Americans and the lowest risk for Latinos. In recent years, however, an increase in risk has been observed for African American men in late life. Rates of suicide among older adults have been declining in the past decade. It is too early to

determine whether the effect is due to prevention activities, such as increased use of antidepressant medication in this age group, or other trends that remain to be identified.

Suicidal behavior in late life differs in several ways from that observed earlier in the lifespan. Older adults tend to use more immediately lethal means, and suicidal behavior is more likely to be fatal among older adults than at any other age. In addition, the suicidal deaths of older adults reflect a higher level of intent and more planning than those of their younger counterparts (Conwell et al. 1998). Older adults are less likely to verbalize suicidal thoughts than are younger or middle-aged adults. In contrast, older adults have been reported to have higher rates of death ideation, such as a passive wish to die. A final important difference between older adults who are suicidal and their younger counterparts is that older adults are particularly likely to visit a physician shortly before the death (Luoma et al. 2002). Among adults who died by suicide at age 55 or older, up to 70% visited a primary care provider within one month of the death.

The predominant risk factor for suicide in late life is depression, which is present in approximately 85% of older adults who die by suicide (Conwell & Brent 1996). Physical illnesses, including cancer, seizure disorder, chronic pulmonary disorder, renal failure, vision or hearing impairment, and even incontinence have also been associated with increased risk of suicide in late life, with effects partially but not fully explained by depression (reviewed by Fiske et al. 2008). Personality characteristics have also been associated with suicidal behavior in late life, including high scores on neuroticism scales and low scores on an openness-to-experience scale (Duberstein et al. 2000). Several investigators have suggested that a rigid personality style, as reflected by low openness to experience, may increase risk for suicide particularly in interaction with the types of events older adults are likely to experience, such as functional impairment and other challenges (Duberstein et al. 2000). Alcohol abuse increases risk for suicide among

**Table 1 Psychological interventions for depression in late life**

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<b>Evidence-based interventions</b>
Behavioral therapy
Cognitive-behavioral therapy
Cognitive bibliotherapy
Problem-solving therapy
Brief psychodynamic therapy
Life review therapy
<b>Promising interventions</b>
Interpersonal therapy <sup>a</sup>
Clinical case management <sup>b</sup>
Personal construct therapy <sup>b</sup>
Coping Together group therapy <sup>b</sup>
Interpersonal counseling <sup>b</sup>
Behavioral bibliotherapy <sup>b</sup>
Goal-focused therapy <sup>b</sup>
<b>Evidence-based interventions for caregivers</b>
Cognitive-behavioral therapy
Multicomponent interventions
<b>Evidence-based interventions for persons with dementia</b>
Behavioral therapy
Social engagement approaches
Sensory/environmental approaches

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<sup>a</sup>Efficacy has been demonstrated for continuation treatment of older adult patients who responded to acute treatment with pharmacotherapy or pharmacotherapy + interpersonal therapy.

<sup>b</sup>Efficacy has been demonstrated by only one study or only one set of investigators.

older adults. Consistent with the high rates of depression found in long-term care, the prospect of impending placement in a skilled nursing facility was identified as a risk factor for suicide in one study (Loebel et al. 1991). Several approaches to preventing suicide among older adults, mostly involving the identification and treatment of depression, have demonstrated effectiveness (see Prevention section below).

## TREATMENTS

### Evidence-Based Treatments

A substantial body of evidence supports the use of various forms of psychotherapy as well as somatic interventions in the treatment of depression in older adults. With respect to pharmacologic treatments, randomized clinical trials with depressed older adults have demonstrated similar efficacy for selective serotonin

reuptake inhibitors, tricyclic antidepressants, and monoamine oxidase inhibitors, with moderate to large effect sizes (for a review, see Beyer 2007). Prognosis for older adults is equivalent to that for middle-aged adults, treatment efficacy has been observed in older adults with medical comorbidities (Pinquart et al. 2006).

A number of psychological treatments for depression in late life meet evidence-based criteria (see **Table 1**). Most of these treatments have a behavioral activation component, which directly addresses the problem of activity limitation; some focus on meaningfulness of the activity; others target the cognitions that may intensify and maintain a depressive episode. These interventions include behavioral therapy, cognitive-behavioral therapy, cognitive bibliotherapy, problem-solving therapy, brief psychodynamic therapy, and life review therapy (reviewed by Scogin et al. 2005). These manualized treatments have all been to some extent adapted for older adults. Life review therapy, which was developed specifically for use with older adults, differs from reminiscence activities more broadly in that it is a structured therapy that has been empirically evaluated. For all of these interventions, moderate to large effect sizes are seen in randomized controlled trials. Interpersonal therapy (known as IPT) has been evaluated in older adult samples in combination with medication, but efficacy as a stand-alone psychological treatment for depression in older adults has not yet been studied. Other promising treatments that have not yet been extensively evaluated in older adults include mindfulness-based psychotherapies such as acceptance and commitment therapy (Hayes et al. 1999) and mindfulness-based cognitive therapy (Segal et al. 2001). Mindfulness-based approaches involve teaching clients to be aware of and to accept their thoughts and feelings rather than to engage in either avoidance or rumination. To the extent that this process results in a reduction in negative affect, through distancing from negative thoughts and feelings, it would interrupt the feedback loop depicted in **Figure 2**.

There is relatively less research evaluating these treatments when patients have life complications including psychiatric and medical co-morbidity. However, clinical observations suggest that evidence-based psychological interventions for older adult depression are effective among the terminally ill (King et al. 2005). Furthermore, treatments that combine empirically supported psychological elements with a focus on accessing community resources to address practical problems may be more effective than either approach alone (Areán et al. 2005).

In the few studies that compare pharmacological and psychological interventions, effect sizes are comparable and may favor psychotherapy (Pinquart et al. 2006). In practice, empirically supported psychological treatments are often combined with pharmacological interventions, but research on combined treatment lags behind practice.

Electroconvulsive therapy (ECT), an evidence-based treatment alternative for depression, is used more often in older adults than in any other age group (Kelly & Zisselman 2000). Treatment efficacy is impressive, with improvement seen in more than 80% of patients in most trials, but adverse events such as cardiac complications, memory loss, and delirium suggest caution in the use of ECT for older adults. Cognitive effects are transient in most but not all cases. Because ECT is most often recommended by clinicians in cases of depression with potentially life-threatening complications, earlier recognition of depression and referral to treatment may reduce the use of ECT.

Cognitive changes complicate treatment options. For example, some research shows poorer response to pharmacotherapy for older adults with white matter hyperintensities on neuroimaging (Taylor et al. 2003), and cognitive-behavioral material may need to be simplified. Yet depression in the context of dementia is amenable to treatment and should be treated. Consensus guidelines describe the outcomes associated with pharmacotherapy as mixed but recommend antidepressant medica-

tions for significant and persistent depressive symptoms (Am. Psychiatr. Assoc. 2007). There is substantial evidence of efficacy for psychosocial treatments, including behavioral and social engagement approaches (Teri et al. 2005). Focus on the caregiver appears to be an important component of behavioral treatment, involving improvement in the caregiver's skills in communicating with the patient and adapting to the disease. Caregivers are instrumental in increasing the patient's engagement in pleasant activities. Both cognitive-behavioral and multicomponent treatment approaches are effective in reducing depression in the caregiver (Gallagher-Thompson & Coon 2007).

In summary, the evidence clearly shows that there are multiple therapeutic alternatives, including somatic and psychotherapeutic approaches, each with demonstrable efficacy for treating depression in late life. Because depression in late life, even at subsyndromal levels, is associated with increased physical impairment (Judd et al. 2002), treatment of depression may provide an opportunity to improve physical function. Clinical trials of depression interventions for older adults have begun to evaluate functioning as an outcome measure. As yet, few studies have considered how individual differences may modify the efficacy of treatments.

Unfortunately, a large proportion of older adults with depression do not receive treatment of any kind, although recent research shows a positive trend (Blazer et al. 2005). Lack of treatment among older adults may reflect, in part, the difficulty of detecting depression in older adults due to age-associated differences in presentation described above. Because depressed older adults are more likely to seek care from a primary care provider than in the specialty mental health sector (Uebelacker et al. 2006), collaborative care models have been developed in which pharmacological and psychological treatments are delivered in primary care settings (Bruce et al. 2004, Unützer et al. 2002) or in the patient's home (Ciechanowski et al. 2004), supervised by a depression care manager. Studies have shown greater improvement, including reduced

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**ECT:**  
electroconvulsive  
therapy

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suicidal ideation, compared to management of depression treatment by the primary care physician alone. These favorable outcomes may be largely attributable to reduced dropout rates when psychological services are colocated in medical settings, highlighting the importance of access to psychological services for depressed older adults (Bartels et al. 2004).

The model of depression held by the depressed older adult and by the general practitioner may also affect whether treatment is sought, whether treatment is offered, and whether there is adherence to the program of treatment. Based on work with mixed-aged depression patients, it is recommended that primary care physicians assess the patients' beliefs about depression and provide education about the role of life stressors in causing depression and the importance of activation to recovery (Brown et al. 2007). Moreover, education about behavioral explanations for depression is generally more effective than education about biomedical explanations (Lam et al. 2005). With older adults, however, it is important not to overemphasize the role of life stressors in such a way that depression is normalized by older adult patients or their physicians. Rather, the importance of behavioral disengagement and self-blame as contributing to depression as well as any biological risk factors that may interact with the psychosocial context need to be addressed.

## New Treatments

Repetitive transcranial magnetic stimulation, a technique in which rapidly changing magnetic fields are used to induce electrical currents in the brain, was not more effective than sham stimulation in two studies of older adults with treatment-resistant depression of diverse etiologies (Manes et al. 2001, Mosimann et al. 2004), but it appears to be effective relative to sham treatment for poststroke and vascular depression (Jorge et al. 2004, 2008) and as effective as fluoxetine for depression in Parkinson's disease (Fregni et al. 2004). Although age did not appear to influence results in the poststroke

sample, older patients in the vascular depression group showed poorer response. Across studies, smaller frontal lobe volume was associated with poorer response.

Some research suggests the efficacy of aerobic exercise as a complementary or alternative treatment for depression among older adults (Sjösten & Kivelä 2006). Weight training may also have an antidepressant effect (Singh et al. 2005). Exercise has been shown to be as effective as antidepressant selective serotonin reuptake inhibitor medication (specifically, sertraline) and more effective than attention placebos such as health lectures or supportive contact for depressed older adults (Barbour & Blumenthal 2005). Exercise is effective even in older people with medication-resistant depression, poststroke depression, and in those with depressive symptoms as well as major depression (Barbour & Blumenthal 2005, Sjösten & Kivelä 2006). Studies with long-term follow-up have found lower relapse rates over as long as five years for those who continue to exercise (Motl et al. 2005).

This literature has been criticized for poor quality methodology, including failure to adequately describe the randomization concealment method and blinding procedure, small samples, and poor data-analytic techniques (Sjösten & Kivelä 2006). These flaws do not appear sufficient to justify disregarding this important body of work. A more serious concern is that depression itself may reduce the appeal of exercise, and therefore the samples recruited for exercise studies may be highly selected and unrepresentative of depressed older adults. Overall, however, exercise appears to be an efficacious treatment for late-life depression, with additional important benefits for health in later life.

## PREVENTION

Prevention efforts may aim to avoid a first onset of depression, a recurrence in late life, or a relapse following treatment. Since over half of older adults with depression have the first onset in late life, it is as appropriate to design

prevention efforts targeting first onsets in this age group as at earlier ages.

Preventive efforts are often targeted at those who are at increased risk of disorder. The most promising preventive approach may be treating older adults with subsyndromal depressive symptoms in order to prevent full-blown disorder. In the Amsterdam Study of the Elderly, the authors calculated that only 5.8 older adults with subsyndromal depressive symptoms needed to be treated in order to prevent one depression onset within three years, and that treatment of all patients with subsyndromal depressive symptoms could prevent 24.6% of new depression onsets in that period (Schoevers et al. 2006).

The treatment of comorbid insomnia or other sleep disturbance may represent a particularly valuable opportunity to prevent future depressive episodes in older adults (Cole & Dendukuri 2003), as insomnia symptoms are a known risk factor for future depressive episodes. Fortunately, cognitive-behavioral treatments for insomnia in this age group are highly effective, even among individuals with secondary insomnia and those who are dependent on sleep medications (Nau et al. 2005).

Other prevention interventions target older adults at risk of depression due to physical illness and disability, bereavement, and caregiver status. Interventions that have the most empirical support include individual therapy for at-risk bereaved older adults, educational interventions for subjects with chronic illness, cognitive-behavioral interventions to reduce negative thinking, and life review (reviewed by Cole 2008). Stroke patients who receive antidepressant medication prophylactically are less likely to become depressed than those who receive placebo (Whyte et al. 2006). Promising strategies for caregivers of ill or disabled persons include group support and skills training. Because depression in this group is strongly associated with restriction of activities, behavioral activation may be a particularly appropriate preventive intervention. Given the association of loneliness to depression among older adults,

programs to reduce social isolation may be of benefit. A telephone support and emergency response program that serves a large number of isolated older adults in Italy, many of whom are in frail health, found that suicide rates over a 10-year period were lower than expected, suggesting that a reduction of depressive symptoms may have occurred (De Leo et al. 2002).

Prevention strategies may also be used to reduce the risk of adverse outcomes of depression in older adults. Screening for suicide risk among older adults with depression, followed by effective depression treatment, reduces suicidal thoughts (Bruce et al. 2004) and may, therefore, reduce risk of suicidal behaviors.

Approaches not targeted according to identified risk factors may also be helpful, including programs that educate professional and lay audiences regarding recognition of depression in older adults, stressing particularly that depression is not a normal part of aging. In an important study that has since been replicated in several other locales, all the primary care physicians on the island of Gotland, Sweden, were trained to detect and respond to depression (Rutz et al. 1992). Rates of diagnosed depression subsequently increased, and rates of suicide decreased. Such training may be particularly helpful in long-term care settings, where high rates of depression may obscure the reality that depression is not inevitable—nor even the norm—in this age group. High rates of depression in skilled nursing facilities could also be taken as a sign that environmental changes are necessary (Zeiss 2005).

## CONCLUSIONS

Empirical literature converges to support the conclusion that depression is not a normal part of aging. Depression is less common in late life than in midlife, except in a more delimited form. Although late-life depression is often less severe, the consequences can be devastating.

Depression in older adults can be understood from a lifespan developmental diathesis-stress perspective. Risk and protective factors become more or less prominent in the etiology

of depression as they change in frequency or importance over the course of the lifespan. Biological risks become dramatically more prevalent in late life, as do certain life events, whereas psychological vulnerability decreases and psychological resilience increases. Considering the biological and social challenges associated with older adulthood, the fact that depressive disorders become less rather than more prevalent in this age group is evidence of the importance of protective factors. The etiological picture of depression in late life is complex. Late-life depression is characterized by heterogeneity, with age of first onset a likely marker of etiological differences. Early-onset depression is influenced by genes for depression, whereas

late onset may represent either a prodrome of dementia or a biological or psychological response to the events that are more common in late life (e.g., physical illness, bereavement, caregiving).

There is substantial consensus regarding broad categories of risk factors for late-life depression, which include most prominently neurological vulnerability, physical illness and disability, and stressful life events such as bereavement and caregiving. Research is only beginning to examine interactions between these risk factors. As the evidence regarding risk and protective factors accumulates, the design and testing of novel preventive approaches becomes possible.

### SUMMARY POINTS

1. Depression is less prevalent among older adults than younger adults, but merits special attention because it can have serious negative consequences, including increased burden of physical illness, impaired functioning, and risk of suicide. More than half of depressed older adults had the first episode after age 60.
2. The presentation of depression differs in older adults compared to younger adults. Older adults are less likely to endorse affective symptoms and more likely to display cognitive changes, somatic symptoms, and loss of interest than are younger adults.
3. Factors leading to the development of late-life depression likely comprise complex interactions of genetic vulnerabilities, cognitive diathesis, and age-associated neurobiological changes with the particular types of stressful events that occur more often in late life.
4. A common pathway to depression in older adults, regardless of whether predisposing risks are biological, psychological, or social, may be curtailment of daily activities. Accompanying self-critical thinking may exacerbate and maintain a depressed state.
5. Age-related increases in psychological strengths, and reductions in psychological vulnerabilities, offset the increasing prevalence of certain risk factors in late life. Other protective factors include higher education and socioeconomic status, good health and cognitive function, engagement in valued activities, and religious involvement.
6. Depression in late life is treatable, even among older adults with dementia. Empirical evidence indicates that behavioral therapy, cognitive-behavioral therapy, cognitive bibliotherapy, problem-solving therapy, brief psychodynamic therapy, and life review/reminiscence therapy are effective but too infrequently used with older adults. Specialized, evidence-based approaches have been developed for individuals with dementia and for caregivers.

7. Emerging evidence supports the use of psychological and somatic interventions to prevent the onset of depression in late life, including cognitive and behavioral interventions for bereaved older adults, individuals with chronic illnesses, and caregivers, and prophylactic antidepressant treatment in individuals who have had a stroke. The adequate treatment of residual symptoms following an acute depressive episode, including insomnia symptoms, may prevent relapse.

## DISCLOSURE STATEMENT

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## LITERATURE CITED

- Alexopoulos GS. 2005. Depression in the elderly. *Lancet* 365:1961–70
- Am. Psychiatr. Assoc. 1994. *Diagnostic and Statistical Manual for Mental Disorders*. Washington, DC: Am. Psychiatr. Assoc. 4th ed.
- Am. Psychiatr. Assoc. 2007. *Practice guideline for the treatment of patients with Alzheimer's disease and other dementias*. Arlington, VA: Am. Psychiatr. Assoc. [http://www.guideline.gov/summary/summary.aspx?doc\\_id=11533&nbr=5974](http://www.guideline.gov/summary/summary.aspx?doc_id=11533&nbr=5974)
- Andreescu C, Lenze EJ, Dew MA, Begley AE, Mulsant BH, et al. 2007. Effect of comorbid anxiety on treatment response and relapse risk in late-life depression: controlled study. *Br. J. Psychiatry* 190:344–49
- Andrew DH, Dulin PL. 2007. The relationship between self-reported health and mental health problems among older adults in New Zealand: experiential avoidance as a moderator. *Aging Ment. Health* 11:596–603
- Areán PA, Gum A, McCulloch CE, Bostrom A, Gallagher-Thompson D, Thompson L. 2005. Treatment of depression in low-income older adults. *Psychol. Aging* 20:601–9
- Barbour KA, Blumenthal JA. 2005. Exercise training and depression in older adults. *Neurobiol. Aging* 26(Suppl. 1):119–23
- Bartels SJ, Coakley EH, Zubritzky C, Ware JH, Miles KM, et al. 2004. Improving access to geriatric mental health services: a randomized trial comparing treatment engagement with integrated versus enhanced referral care for depression, anxiety, and at-risk alcohol use. *Am. J. Psychiatry* 161:1455–62
- Beekman AT, de Beurs E, van Balkom AJ, Deeg DJ, van Dyck R, van Tilburg W. 2000. Anxiety and depression in later life: co-occurrence and communality of risk factors. *Am. J. Psychiatry* 157:89–95
- Benyamini Y, Lomranz J. 2004. The relationship of activity restriction and replacement with depressive symptoms among older adults. *Psychol. Aging* 19:362–66
- Beyer JL. 2007. Managing depression in geriatric populations. *Ann. Clin. Psychiatry* 19:221–28
- Blazer DG. 2003. Depression in late life: review and commentary. *J. Gerontol. A Biol. Sci. Med. Sci.* 58:249–65
- Blazer DG, Hybels CF, Fillenbaum GG, Pieper CF. 2005. Predictors of antidepressant use among older adults: Have they changed over time? *Am. J. Psychiatry* 162:705–10
- Blumstein T, Benyamini Y, Fuchs Z, Shapira Z, Novikov I, et al. 2004. The effect of a communal lifestyle on depressive symptoms in late life. *J. Aging Health* 16:151–74

- Bostwick JM, Pankratz VS. 2000. Affective disorders and suicide risk: a reexamination. *Am. J. Psychiatry* 157:1925-32
- Brodsky H, Luscombe G, Parker G, Wilhelm K, Hickie I, et al. 2001. Early and late onset depression in old age: different aetiologies, same phenomenology. *J. Affect. Disord.* 66:225-36
- Brown C, Battista DR, Sereika SM, Bruhlman RD, Dunbar-Jacob J, Thase ME. 2007. Primary care patients' personal illness models for depression: relationship to coping behavior and functional disability. *Gen. Hosp. Psychiatry* 29:492-500
- Bruce ML, McAvay GJ, Raue PJ, Brown EL, Meyers BS, et al. 2002. Major depression in elderly home health care patients. *Am. J. Psychiatry* 159:1367-74
- Bruce ML, Ten Have TR, Reynolds CF III, Katz IR, Schulberg HC, et al. 2004. Reducing suicidal ideation and depressive symptoms in depressed older primary care patients: a randomized controlled trial. *JAMA* 291:1081-91
- Butters MA, Becker JT, Nebes RD, Zmuda MD, Mulsant BH, et al. 2000. Changes in cognitive functioning following treatment of late life depression. *Am. J. Psychiatry* 157:1949-54
- Butters MA, Whyte EM, Nebes RD, Begley AE, Dew MA, et al. 2004. The nature and determinants of neuropsychological functioning in late-life depression. *Arch. Gen. Psychiatry* 61:587-95
- Butterworth P, Gill SC, Rodgers B, Anstey KJ, Villamil E, Melzer D. 2006. Retirement and mental health: analysis of the Australian national survey of mental health and well-being. *Soc. Sci. Med.* 62:1179-91
- Carney RM, Freedland KE. 2003. Depression, mortality, and medical morbidity in patients with coronary heart disease. *Biol. Psychiatry* 54:241-47
- Carstensen LL, Fung HH, Charles ST. 2003. Socioemotional selectivity theory and the regulation of emotion in the second half of life. *Motiv. Emot.* 27:103-23
- Cervilla J, Prince M, Joels S, Russ C, Lovestone S. 2004. Genes related to vascular disease (APOE, VLDL-R, DCP-1) and other vascular factors in late-life depression. *Am. J. Geriatr. Psychiatry* 12:202-10
- Charles ST, Reynolds CA, Gatz M. 2001. Age-related differences and change in positive and negative affect over 23 years. *J. Personal. Soc. Psychol.* 80:136-51
- Charlson M, Peterson JC. 2002. Medical comorbidity and late life depression: What is known and what are the unmet needs? *Biol. Psychiatry* 52:226-35
- Chow SM, Hamagami F, Nesselroade JR. 2007. Age differences in dynamical emotion-cognition linkages. *Psychol. Aging* 22:765-80
- Christensen H, Jorm AF, Mackinnon AJ, Korten AE, Jacomb PA, et al. 1999. Age differences in depression and anxiety symptoms: a structural equation modelling analysis of data from a general population sample. *Psychol. Med.* 29:325-39
- Ciechanowski P, Wagner E, Schmalting K, Schwartz S, Williams B, et al. 2004. Community-integrated home-based depression treatment in older adults: a randomized controlled trial. *JAMA* 291:1569-77
- Cole MG. 2008. Brief interventions to prevent depression in older subjects: a systematic review of feasibility and effectiveness. *Am. J. Geriatr. Psychiatry* 16:435-43
- Cole MG, Dendukuri N. 2003. Risk factors for depression among elderly community subjects: a systematic review and meta-analysis. *Am. J. Psychiatry* 160:1147-56
- Conwell Y, Brent D. 1996. Suicide and aging I: patterns of psychiatric diagnosis. In *Suicide: International Perspectives*, ed. JL Pearson, Y Conwell, pp. 15-30. New York: Springer
- Conwell Y, Duberstein PR, Cox C, Hermann J, Forbes N, Caine ED. 1998. Age differences in behaviors leading to completed suicide. *Am. J. Geriatr. Psychiatry* 6:122-26
- De Leo D, Dello Buono M, Dwyer J. 2002. Suicide among the elderly: the long-term impact of a telephone support and assessment intervention in northern Italy. *Br. J. Psychiatry* 181:226-29
- DeLuca AK, Lenze EJ, Mulsant BH, Butters MA, Karp JF, et al. 2005. Comorbid anxiety disorder in late life depression: association with memory decline over four years. *Int. J. Geriatr. Psychiatry* 20:848-54
- Djernes JK. 2006. Prevalence and predictors of depression in populations of elderly: a review. *Acta Psychiatr. Scand.* 113:372-87
- Duberstein PR, Conwell Y, Seidlitz L, Denning D, Cox C, Caine ED. 2000. Personality traits and suicidal behavior and ideation in depressed inpatients 50 years of age and older. *J. Gerontol. B Psychol. Sci. Soc. Sci.* 55:18-26

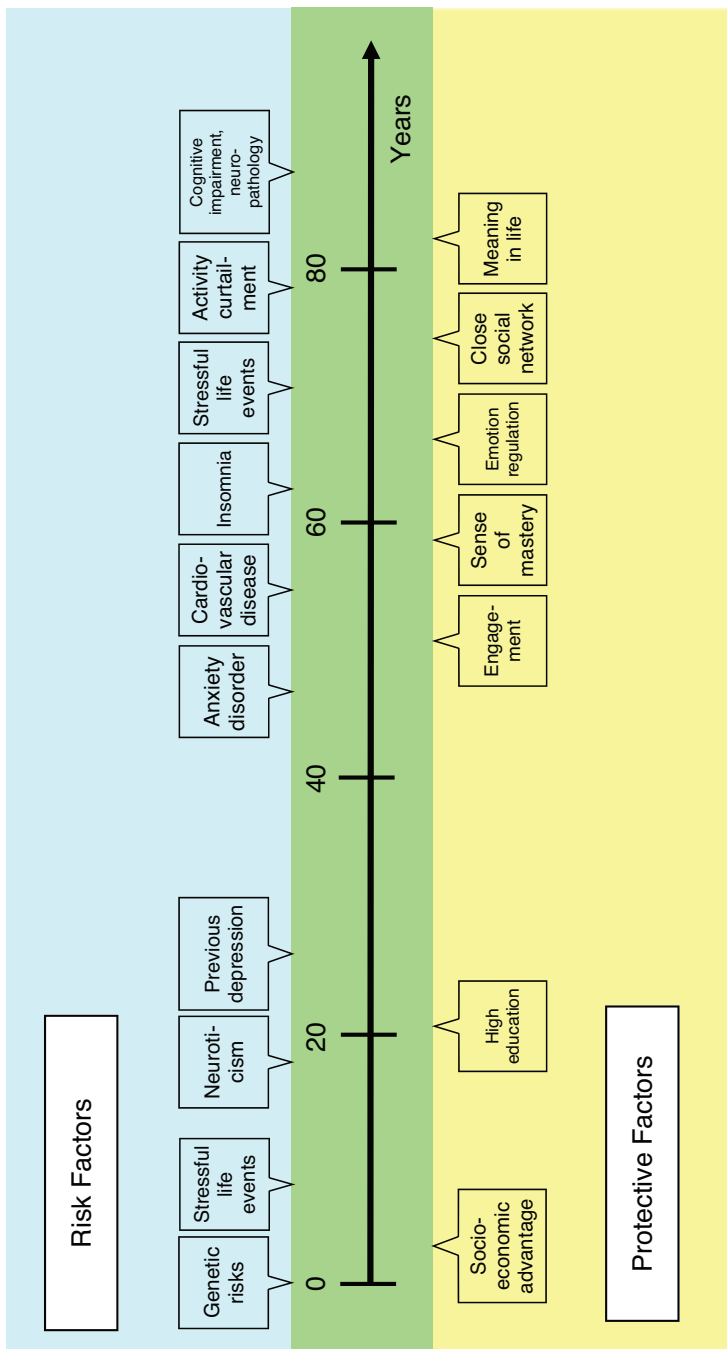
- Ehrt U, Brønnick K, Leentjens AF, Larsen JP, Aarsland D. 2006. Depressive symptom profile in Parkinson's disease: a comparison with depression in elderly patients without Parkinson's disease. *Int. J. Geriatr. Psychiatry* 21:252–58
- Engum A. 2007. The role of depression and anxiety in onset of diabetes in a large population-based study. *J. Psychosom. Res.* 62:31–38
- Fiske A, Gatz M, Pedersen NL. 2003. Depressive symptoms and aging: the effects of illness and non-health-related events. *J. Gerontol. B Psychol. Sci. Soc. Sci.* 58:P320–28
- Fiske A, O'Riley AA, Widoe RK. 2008. Physical health and suicide in late life. *Clin. Gerontol.* 31:31–50
- Fregni F, Santos CM, Myczkowski ML, Rigolino R, Gallucci-Neto J, et al. 2004. Repetitive transcranial magnetic stimulation is as effective as fluoxetine in the treatment of depression in patients with Parkinson's disease. *J. Neurol. Neurosurg. Psychiatry* 75:1171–74
- Gallagher-Thompson D, Coon DW. 2007. Evidence-based psychological treatments for distress in family caregivers of older adults. *Psychol. Aging* 22:37–51
- Gallo JJ, Anthony JC, Muthén BO. 1994. Age differences in the symptoms of depression: a latent trait analysis. *J. Gerontol.* 49:P251–64
- Gallo JJ, Cooper-Patrick L, Lesikar S. 1998. Depressive symptoms of whites and African Americans aged 60 years and older. *J. Gerontol. B Psychol. Sci. Soc. Sci.* 53:P277–86
- Gallo JJ, Rabins PV, Lyketsos CG, Tien AY, Anthony JC. 1997. Depression without sadness: functional outcomes of nondysphoric depression in later life. *J. Am. Geriatr. Soc.* 45:570–78
- Garnefski N, Kraaij V. 2006. Relationships between cognitive emotion regulation strategies and depressive symptoms: a comparative study of five specific samples. *Personal. Individ. Differ.* 40:1659–69
- Geda YE, Knopman DS, Mrazek DA, Jicha GA, Smith GE, et al. 2006. Depression, apolipoprotein E genotype, and the incidence of mild cognitive impairment: a prospective cohort study. *Arch. Neurol.* 63:435–40
- Gehi A, Haas D, Pipkin S, Whooley MA. 2005. Depression and medication adherence in outpatients with coronary heart disease: findings from the Heart and Soul Study. *Arch. Intern. Med.* 165:2508–13
- George LK, Ellison CG, Larson DB. 2002. Explaining the relationships between religious involvement and health. *Psychol. Inq.* 13:190–200
- Golden SH, Lazo M, Carnethon M, Bertoni AG, Schreiner PJ, et al. 2008. Examining a bidirectional association between depressive symptoms and diabetes. *JAMA* 299:2751–59
- Goodwin RD, Devanand DP. 2008. Stroke, depression, and functional health outcomes among adults in the community. *J. Geriatr. Psychiatry Neurol.* 21:41–46
- Green RC, Cupples LA, Kurz A, Auerbach S, Go R, et al. 2003. Depression as a risk factor for Alzheimer disease: the MIRAGE Study. *Arch. Neurol.* 60:753–59
- Hammen CL. 1991. The generation of stress in the course of unipolar depression. *J. Abnorm. Psychol.* 100:555–61
- Hasin DS, Goodwin RD, Stinson FS, Grant BF. 2005. Epidemiology of major depressive disorder: results from the National Epidemiologic Survey on Alcoholism and Related Conditions. *Arch. Gen. Psychiatry* 62:1097–106
- Hayes SC, Strosahl KD, Wilson KG. 1999. *Acceptance and Commitment Therapy: An Experiential Approach to Behavior Change*. New York: Guilford
- Hendrie HC, Albert MS, Butters MA, Gao S, Knopman DS, et al. 2006. The NIH Cognitive and Emotional Health Project: report of the Critical Evaluation Study Committee. *Alzheimer's Dement.* 2:12–32
- Hettema JM, Kuhn JW, Prescott CA, Kendler KS. 2006. The impact of generalized anxiety disorder and stressful life events on risk for major depressive episodes. *Psychol. Med.* 36:789–95
- Heun R, Papassotiropoulos A, Jessen F, Maier W, Breitner JC. 2001. A family study of Alzheimer disease and early- and late-onset depression in elderly patients. *Arch. Gen. Psychiatry* 58:190–96
- Hickie I, Scott E, Naismith S, Ward P, Turner K, et al. 2001. Late-onset depression: genetic, vascular and clinical contributions. *Psychol. Med.* 31:1403–12
- Hwang JP, Yang CH, Hong CJ, Lirng JF, Yang YM, Tsai SJ. 2006. Association of APOE genetic polymorphism with cognitive function and suicide history in geriatric depression. *Dement. Geriatr. Cogn. Disord.* 22:334–38
- Ishihara L, Brayne C. 2006. A systematic review of depression and mental illness preceding Parkinson's disease. *Acta Neurol. Scand.* 113:211–20

- Jansson M, Gatz M, Berg S, Johansson B, Malmberg B, et al. 2003. Association between depressed mood in the elderly and a 5-HTT2A gene variant. *Am. J. Med. Genet. B Neuropsychiatr. Genet.* 120B:79–84
- Jeste ND, Hays JC, Steffens DC. 2006. Clinical correlates of anxious depression among elderly patients with depression. *J. Affect. Disord.* 90:37–41
- Jorge RE, Moser DJ, Acion L, Robinson RG. 2008. Treatment of vascular depression using repetitive transcranial magnetic stimulation. *Arch. Gen. Psychiatry* 65:268–76
- Jorge RE, Robinson RG, Tateno A, Narushima K, Acion L, et al. 2004. Repetitive transcranial magnetic stimulation as treatment of poststroke depression: a preliminary study. *Biol. Psychiatry* 55:398–405
- Jorm AF. 2001. History of depression as a risk factor for dementia: an updated review. *Aust. N. Z. J. Psychiatry* 35:776–81
- Judd LL, Schettler PJ, Akiskal HS. 2002. The prevalence, clinical relevance, and public health significance of subthreshold depressions. *Psychiatr. Clin. North Am.* 25:685–98
- Kelly KG, Zisselman M. 2000. Update on electroconvulsive therapy (ECT) in older adults. *J. Am. Geriatr. Soc.* 48:560–66
- Kendler KS, Gatz M, Gardner CO, Pedersen NL. 2005. Age at onset and familial risk for major depression in a Swedish national twin sample. *Psychol. Med.* 35:1573–79
- Kendler KS, Gatz M, Gardner CO, Pedersen NL. 2006a. A Swedish national twin study of lifetime major depression. *Am. J. Psychiatry* 163:109–14
- Kendler KS, Gatz M, Gardner CO, Pedersen NL. 2006b. Personality and major depression: a Swedish longitudinal population-based twin study. *Arch. Gen. Psychiatry* 63:1113–20
- King DA, Heisel MJ, Lyness JF. 2005. Assessment and psychological treatment of depression in older adults with terminal or life-threatening illness. *Clin. Psychol. Sci. Pract.* 12:339–53
- Knight BG, Flynn Longmire CV, Dave J, Kim JH, David S. 2007. Mental health and physical health of family caregivers for persons with dementia: a comparison of African American and white caregivers. *Aging Ment. Health* 11:538–46
- Kockler M, Heun R. 2002. Gender differences of depressive symptoms in depressed and nondepressed elderly persons. *Int. J. Geriatr. Psychiatry* 17:65–72
- Krishnan KR. 2002. Biological risk factors in late life depression. *Biol. Psychiatry* 52:185–92
- Krishnan KR, DeLong M, Kraemer H, Carney R, Spiegel D, et al. 2002. Comorbidity of depression with other medical diseases in the elderly. *Biol. Psychiatry* 52:559–88
- Krishnan KR, Tupler LA, Ritchie JC Jr, McDonald WM, Knight DL, et al. 1996. Apolipoprotein E-epsilon 4 frequency in geriatric depression. *Biol. Psychiatry* 40:69–71
- Kung H-S, Hoyert DL, Xu J, Murphy SL. 2008. *Deaths: final data for 2005*. National Vital Statistics Reports. Vol. 56, No. 10. Hyattsville, MD: Nat. Cent. Health Statist. [http://www.cdc.gov/nchs/data/nvsr/nvsr56/nvsr56\\_10.pdf](http://www.cdc.gov/nchs/data/nvsr/nvsr56/nvsr56_10.pdf)
- Lam DCK, Salkovskis PM, Warwick HMC. 2005. An experimental investigation of the impact of biological versus psychological explanations of the cause of mental illness. *J. Mental Health* 14:453–64
- Lenze EJ, Minin JC, Ferrell RE, Pollock BG, Skidmore E, et al. 2005. Association of the serotonin transporter gene-linked polymorphic region (5-HTTLPR) genotype with depression in elderly persons after hip fracture. *Am. J. Geriatr. Psychiatry* 13:428–32
- Lenze EJ, Mulsant BH, Shear MK, Schulberg HC, Dew MA, et al. 2000. Comorbid anxiety disorders in depressed elderly patients. *Am. J. Psychiatry* 157:722–28
- Lewinsohn PM, Muñoz RF, Youngren MA, Zeiss AM. 1986. *Control Your Depression*. New York: Prentice Hall. 2nd ed.
- Li C, Ford ES, Strine TW, Mokdad AH. 2008. Prevalence of depression among U.S. adults with diabetes: findings from the 2006 Behavioral Risk Factor Surveillance System. *Diabetes Care* 31:105–7
- Lichstein KL, Stone KC, Nau SD, McCrae CS, Payne KL. 2006. Insomnia in the elderly. *Sleep Med. Clin.* 1:221–29
- Loebel JP, Loebel JS, Dager SR, Centerwall BS, Reay DT. 1991. Anticipation of nursing home placement may be a precipitant of suicide among the elderly. *J. Am. Geriatr. Soc.* 39:407–8
- Luoma JB, Martin CE, Pearson JL. 2002. Contact with mental health and primary care providers before suicide: a review of the evidence. *Am. J. Psychiatry* 159:909–16

- Manber R, Edinger JD, Gress JL, San Pedro-Salcedo MG, Kuo TF, Kalista T. 2008. Cognitive behavioral therapy for insomnia enhances depression outcome in patients with comorbid major depressive disorder and insomnia. *Sleep* 31:489–95
- Manes F, Jorge R, Morcuende M, Yamada T, Paradiso S, Robinson RG. 2001. A controlled study of repetitive transcranial magnetic stimulation as a treatment of depression in the elderly. *Int. Psychogeriatr.* 13:225–31
- Maraldi C, Volpato S, Penninx BW, Yaffe K, Simonsick EM, et al. 2007. Diabetes mellitus, glycemic control, and incident depressive symptoms among 70- to 79-year-old persons: the health, aging, and body composition study. *Arch. Intern. Med.* 167:1137–44
- Marsh L, McDonald WM, Cummings J, Ravina B, NINDS/NIMH Work Group on Depression and Parkinson's Disease. 2006. Provisional diagnostic criteria for depression in Parkinson's disease: report of an NINDS/NIMH Work Group. *Mov. Disord.* 21:148–58
- Mazure CM, Maciejewski PK, Jacobs SC, Bruce ML. 2002. Stressful life events interacting with cognitive/personality styles to predict late-onset major depression. *Am. J. Geriatr. Psychiatry* 10:297–304
- Mojtabai R, Olfson M. 2004. Major depression in community-dwelling middle-aged and older adults: prevalence and 2-year and 4-year follow-up symptoms. *Psychol. Med.* 34:623–34
- Mosimann UP, Schmitt W, Greenberg BD, Kosel M, Müri RM, et al. 2004. Repetitive transcranial magnetic stimulation: a putative add-on treatment for major depression in elderly patients. *Psychiatry Res.* 126:123–33
- Motl RW, Konopack JF, McAuley E, Elavsky S, Jerome GJ, Marquez DX. 2005. Depressive symptoms among older adults: long-term reduction after a physical activity intervention. *J. Behav. Med.* 28:385–94
- Naarding P, Schoevers RA, Janzing JG, Jonker C, Koudstaal PJ, Beekman AT. 2005. A study on symptom profiles of late-life depression: the influence of vascular, degenerative and inflammatory risk-indicators. *J. Affect. Disord.* 88:155–62
- Nagurney AJ, Reich JW, Newsom JT. 2004. Gender moderates the effects of independence and dependence desires during the social support process. *Psychol. Aging* 19:215–8
- Nau SD, McCrae CS, Cook KG, Lichstein KL. 2005. Treatment of insomnia in older adults. *Clin. Psychol. Rev.* 25:645–72
- Neupert SD, Almeida DM, Charles ST. 2007. Age differences in reactivity to daily stressors: the role of personal control. *J. Gerontol. B Psychol. Sci. Soc. Sci.* 62:P216–25
- Newmann JP. 1989. Aging and depression. *Psychol. Aging* 4:150–65
- Newmann JP, Engel RJ, Jensen JE. 1991. Age differences in depressive symptom experiences. *J. Gerontol.* 46:P224–35
- Nolen-Hoeksema S, Ahrens C. 2002. Age differences and similarities in the correlates of depressive symptoms. *Psychol. Aging* 17:116–24
- Nolen-Hoeksema S, Davis CG. 1999. “Thanks for sharing that”: ruminators and their social support networks. *J. Personal. Soc. Psychol.* 4:801–14
- Olin JT, Schneider LS, Katz IR, Meyers BS, Alexopoulos GS, et al. 2002. Provisional diagnostic criteria for depression of Alzheimer disease. *Am. J. Geriatr. Psychiatry* 10:125–28
- Otte C, McCaffery J, Ali S, Whooley MA. 2007. Association of a serotonin transporter polymorphism (5-HTTLPR) with depression, perceived stress, and norepinephrine in patients with coronary disease: The Heart and Soul Study. *Am. J. Psychiatry* 164:1379–84
- Owby RL, Crocco E, Acevedo A, John V, Loewenstein D. 2006. Depression and risk for Alzheimer disease: systematic review, meta-analysis, and meta-regression analysis. *Arch. Gen. Psychiatry* 63:530–38
- Paradiso S, Vaidya J, Tranel D, Kosier T, Robinson RG. 2008. Nondysphoric depression following stroke. *Neuropsychiatry Clin. Neurosci.* 20:52–61
- Park JH, Lee SB, Lee TJ, Lee DY, Jhoo JH, et al. 2007. Depression in vascular dementia is quantitatively and qualitatively different from depression in Alzheimer's disease. *Dement. Geriatr. Cogn. Disord.* 23:67–73
- Perlis ML, Smith LJ, Lyness JM, Matteson SR, Pigeon WR, et al. 2006. Insomnia as a risk factor for onset of depression in the elderly. *Behav. Sleep Med.* 4:104–13
- Piazza JR, Charles ST, Almeida DM. 2007. Living with chronic health conditions: age differences in affective well-being. *J. Gerontol. B Psychol. Sci. Soc. Sci.* 62:P313–21
- Pinquart M, Duberstein PR, Lyness JM. 2006. Treatments for later-life depressive conditions: a meta-analytic comparison of pharmacotherapy and psychotherapy. *Am. J. Psychiatry* 163:1493–501

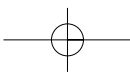
- Prigerson HG, Frank E, Kasl SV, Reynolds CF, Anderson B, et al. 1995. Complicated grief and bereavement-related depression as distinct disorders: preliminary empirical validation in elderly bereaved spouses. *Am. J. Psychiatry* 152:22–30
- Ravina B, Camicioli R, Como PG, Marsh L, Jankovic J, et al. 2007. The impact of depressive symptoms in early Parkinson disease. *Neurology* 69:342–47
- Reijnders JS, Ehrt U, Weber WE, Aarsland D, Leentjens AF. 2008. A systematic review of prevalence studies of depression in Parkinson's disease. *Mov. Disord.* 23:183–89
- Ruscio J, Zimmerman M, McGlinchey JB, Chelminski I, Young D. 2007. Diagnosing major depressive disorder XI: a taxometric investigation of the structure underlying DSM-IV symptoms. *J. Nerv. Ment. Dis.* 195:10–19
- Rutz W, von Knorring L, Wälinder J. 1992. Long-term effects of an educational program for general practitioners given by the Swedish Committee for the Prevention and Treatment of Depression. *Acta Psychiatr. Scand.* 85:83–88
- Schoevers RA, Beekman AT, Deeg DJ, Jonker C, van Tilburg W. 2003. Comorbidity and risk-patterns of depression, generalised anxiety disorder and mixed anxiety-depression in later life: results from the AMSTEL study. *Int. J. Geriatr. Psychiatry* 18:994–1001
- Schoevers RA, Smit F, Deeg DJH, Cuijpers P, Dekker J, et al. 2006. Prevention of late-life depression in primary care: Do we know where to begin? *Am. J. Psychiatry* 163:1611–21
- Schulz R, McGinnis KA, Zhang S, Martire LM, Hebert RS, et al. 2008. Dementia patient suffering and caregiver depression. *Alzheimer Dis. Assoc. Disord.* 22:170–76
- Schweitzer I, Tuckwell V, O'Brien J, Ames D. 2002. Is late onset depression a prodrome to dementia? *Int. J. Geriatr. Psychiatry* 17:997–1005
- Scogin F, Welsh D, Hanson A, Stump J, Coates A. 2005. Evidence-based psychotherapies for depression in older adults. *Psychol. Sci. Pract.* 12:222–37
- Segal ZV, Williams JMG, Teasdale JD, Kabat-Zinn J. 2001. *Mindfulness-Based Cognitive Therapy for Depression: A New Approach to Preventing Relapse*. New York: Guilford
- Singh NA, Stavrinou TM, Scarbek Y, Galambos G, Liber C, Fiatarone Singh MA. 2005. A randomized controlled trial of high- versus low-intensity weight training versus general practitioner care for clinical depression in older adults. *J. Gerontol. A Biol. Sci. Med. Sci.* 60:768–76
- Sjösten N, Kivelä SL. 2006. The effects of physical exercise on depressive symptoms among the aged: a systematic review. *Int. J. Geriatr. Psychiatry* 21:410–18
- Swenson CJ, Baxter J, Shetterly SM, Scarbro SL, Hamman RF. 2000. Depressive symptoms in Hispanic and non-Hispanic white rural elderly. The San Luis Valley Health and Aging Study. *Am. J. Epidemiol.* 152:1048–55
- Taylor W, Steffens D, MacFall J, McQuoid D, Payne M, et al. 2003. White matter hyperintensity progression and late-life depression outcomes. *Arch. Gen. Psychiatry* 60:1090–96
- Teri L, McKenzie G, LaFazia D. 2005. Psychosocial treatment of depression in older adults with dementia. *Clin. Psychol. Sci. Pract.* 12:303–16
- Tiemeier H. 2003. Biological risk factors for late life depression. *Eur. J. Epidemiol.* 18:745–50
- Torges CM, Stewart AJ, Nolen-Hoeksema S. 2008. Regret resolution, aging, and adapting to loss. *Psychol. Aging* 23:169–80
- Uebelacker LA, Wang PS, Berglund P, Kessler RC. 2006. Clinical differences among patients treated for mental health problems in general medical and specialty mental health settings in the National Comorbidity Survey Replication. *Gen. Hosp. Psychiatry* 28:387–95
- Umberson D, Wortman CB, Kessler RC. 1992. Widowhood and depression: explaining long-term gender differences in vulnerability. *J. Health Soc. Behav.* 33:10–24
- Unützer J, Katon W, Callahan CM, Williams JW Jr, Hunkeler E, et al. 2002. Collaborative care management of late-life depression in the primary care setting: a randomized controlled trial. *JAMA* 288:2836–45
- Vink D, Aartsen MJ, Schoevers RA. 2008. Risk factors for anxiety and depression in the elderly: a review. *J. Affect. Disord.* 106:29–44
- Wetherell JL, Gatz M, Pedersen NL. 2001. A longitudinal analysis of anxiety and depressive symptoms. *Psychol. Aging* 16:187–95

- Whooley MA, Caska CM, Hendrickson BE, Rourke MA, Ho J, Ali S. 2007. Depression and inflammation in patients with coronary heart disease: findings from the Heart and Soul Study. *Biol. Psychiatry* 62:314–20
- Whyte EM, Mulsant BH, Rovner BW, Reynolds CF. 2006. Preventing depression after stroke. *Int. Rev. Psychiatry* 18:471–81
- Williamson GM, Shaffer DR. 2000. The activity restriction model of depressed affect: antecedents and consequences of restricted normal activities. In *Physical Illness and Depression in Older Adults: A Handbook of Theory, Research, and Practice*, ed. GM Williamson, DR Shaffer, PA Parmelee, pp. 173–200. New York: Kluwer Acad./Plenum
- Wouts L, Oude Voshaar RC, Bremmer MA, Buitelaar JK, Penninx BW, Beekman AT. 2008. Cardiac disease, depressive symptoms, and incident stroke in an elderly population. *Arch. Gen. Psychiatry* 65:596–602
- Wrosch C, Schulz R, Miller GE, Lupien S, Dunne E. 2007. Physical health problems, depressive mood, and cortisol secretion in old age: buffer effects of health engagement control strategies. *Health Psychol.* 26:341–49
- Yang Y. 2006. How does functional disability affect depressive symptoms in late life? The role of perceived social support and psychological resources. *J. Health Soc. Behav.* 47:355–72
- Zeiss AM. 2005. Depression in long-term care: contrasting a disease model with attention to environmental impact. *Clin. Psychol. Sci. Pract.* 12:300–2
- Zisook S, Kendler KS. 2007. Is bereavement-related depression different than non-bereavement-related depression? *Psychol. Med.* 37:779–94



**Figure 1**

Lifespan perspective on risk and protective factors for late-life major depression. Schematic illustrates the emergence of factors over the lifespan.





# Contents

Construct Validity: Advances in Theory and Methodology <i>Milton E. Strauss and Gregory T. Smith</i> .....	1
Item Response Theory and Clinical Measurement <i>Steven P. Reise and Niels G. Waller</i> .....	27
Methodological Issues in Molecular Genetic Studies of Mental Disorders <i>Carrie E. Bearden, Anna J. Jasinska, and Nelson B. Freimer</i> .....	49
Statistical Methods for Risk-Outcome Research: Being Sensitive to Longitudinal Structure <i>David A. Cole and Scott E. Maxwell</i> .....	71
Psychological Treatment of Anxiety: The Evolution of Behavior Therapy and Cognitive-Behavior Therapy <i>S. Rachman</i> .....	97
Computer-Aided Psychological Treatments: Evolving Issues <i>Isaac Marks and Kate Cavanagh</i> .....	121
The Past, Present, and Future of HIV Prevention: Integrating Behavioral, Biomedical, and Structural Intervention Strategies for the Next Generation of HIV Prevention <i>Mary Jane Rotheram-Borus, Dallas Swendeman, and Gary Chovnick</i> .....	143
Evolving Prosocial and Sustainable Neighborhoods and Communities <i>Anthony Biglan and Erika Hinds</i> .....	169
Five-Factor Model of Personality Disorder: A Proposal for DSM-V <i>Thomas A. Widiger and Stephanie N. Mullins-Sweatt</i> .....	197
Differentiating the Mood and Anxiety Disorders: A Quadripartite Model <i>David Watson</i> .....	221
When Doors of Perception Close: Bottom-Up Models of Disrupted Cognition in Schizophrenia <i>Daniel C. Javitt</i> .....	249

The Treatment of Borderline Personality Disorder: Implications of Research on Diagnosis, Etiology, and Outcome <i>Joel Paris</i> .....	277
Development and Etiology of Disruptive and Delinquent Behavior <i>Rolf Loeber, Jeffrey D. Burke, and Dustin A. Pardini</i> .....	291
Anxiety Disorders During Childhood and Adolescence: Origins and Treatment <i>Ronald M. Rapee, Carolyn A. Schniering, and Jennifer L. Hudson</i> .....	311
APOE-4 Genotype and Neurophysiological Vulnerability to Alzheimer's and Cognitive Aging <i>Susan Bookheimer and Alison Burggren</i> .....	343
Depression in Older Adults <i>Amy Fiske, Julie Loebach Wetherell, and Margaret Gatz</i> .....	363
Pedophilia <i>Michael C. Seto</i> .....	391
Treatment of Smokers with Co-occurring Disorders: Emphasis on Integration in Mental Health and Addiction Treatment Settings <i>Sharon M. Hall and Judith J. Prochaska</i> .....	409
Environmental Influences on Tobacco Use: Evidence from Societal and Community Influences on Tobacco Use and Dependence <i>K. Michael Cummings, Geoffrey T. Fong, and Ron Borland</i> .....	433
Adolescent Development and Juvenile Justice <i>Laurence Steinberg</i> .....	459
<b>Indexes</b>	
Cumulative Index of Contributing Authors, Volumes 1–5 .....	487
Cumulative Index of Chapter Titles, Volumes 1–5 .....	489
<b>Errata</b>	
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