Depression Among Older Adults: A 20-Year Update on Five Common Myths and Misconceptions

Emily A.P. Haigh, Ph.D., Olivia E. Bogucki, M.A., Sandra T. Sigmon, Ph.D., Dan G. Blazer, M.D., Ph.D.

Is depression among older adults symptomatically different than younger adults? Is it more common or chronic or difficult to treat? Is depression in late life more likely to be attributed to psychological problems? Twenty-years ago, Dan Blazer, a pioneer known for his groundbreaking work on depression in older adulthood, conducted an important review of the existing literature to refute five commonly held beliefs about depression in late life. Now, two decades later, we call upon selected articles that are representative of our current knowledge to provide an update and identify research priorities. The research consensus spanning the past 20 years suggests that when compared with their younger counterparts, depression in older adults is not more common and is not more often caused by psychological factors. Although some studies have suggested that depression in late life may be symptomatically different and characterized by a more somatic presentation, there is insufficient empirical evidence to conclude that depression presents differently across adulthood. Overall, older adults respond to psychological interventions as well as younger adults, although evidence suggests that antidepressants are less efficacious in late life. Finally, compared with middle-aged adults, depression in older adults is associated with a more chronic course (i.e., higher rate of relapse), which is likely moderated by medical comorbidity. This special article summarizes our current understanding of the nature and treatment of late-life depression and highlights areas of inquiry in need of further study. (Am J Geriatr Psychiatry 2018; 26:107–122)

Key Words: Older adults, late-life, geriatric, depression, depressive disorders

Highlights

- Compared to younger adults, is MDD in older adults symptomatically different, more common, difficult to treat, chronic, and more often caused by psychological factors?
- MDD is less common in late-life, but has a more chronic course than younger adults. Older adults with subclinical depression report functional impairment similar to MDD.

Received April 7, 2017; revised June 14, 2017; accepted June 14, 2017. From the Department of Psychology (EAPH, OEB, STS), University of Maine, Orono, ME; and the Duke University Medical Center (DGB), Durham, NC. Send correspondence and reprint requests to Emily Haigh, Department of Psychology, University of Maine, Orono, ME 04469. e-mail: emily.a.haigh@maine.edu

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- Depression in late-life may be symptomatically different but more research is needed to separate impact of medical comorbidity.
- Older adults respond to treatment as well as younger adults; antidepressants may be less efficacious in late-life, while older age is a favorable predictor of ECT response.
- While older adults may benefit from enhanced ability to regulate emotions, research suggests that several age-related biological processes contribute to MDD in late-life.

Twenty years ago, Dan Blazer,[1] a pioneer known for his groundbreaking work on depression in late life,[2] challenged five commonly held myths and misconceptions about major depressive disorder (MDD) in older adulthood. Blazer's paper considered several complex issues including whether depression in older adulthood is symptomatically different, more common, more chronic, more difficult to treat, and more often caused by psychological factors than depression at younger ages. The goal of the current article is to revisit, unpack, and update these core issues and highlight priorities for future investigation. To provide comprehensive coverage, articles were selected according to the following search strategy. Titles and abstracts from two databases, MEDLINE and PSYCINFO, were reviewed from 1997 to June 2017, with keywords *depression, depressive disorder, major depressive disorder, geriatric aging*, and *late-life*. Among them, work published in English on the diagnosis, etiology, prevalence, incidence, prognosis, and management of late-life depression were selected. A focus was placed on empirical studies, meta-analyses, and authoritative reviews. Reference lists of the identified papers were examined for further leads. The final selection of articles was based on relevance as judged by the authors.

MYTH 1: DEPRESSION IN LATE LIFE IS SYMPTOMATICALLY DIFFERENT FROM DEPRESSION AT YOUNGER AGES

It has long been debated whether the somatic, cognitive, and emotional symptoms associated with depression present differently across the lifespan. As Blazer[1] noted, many believe late-life depression (defined as depression in those aged ≥65 years) is characterized by more frequent somatic symptoms and cognitive impairments and less frequent emotional symptoms. Twenty years ago, based on the best available evidence (i.e., a study comparing symptoms of MDD among younger and older adult inpatients[3] and community-based studies showing that adults of all ages report similar depressive symptoms on the Center for Epidemiologic Studies of Depression Scale[4] that result in similar factor structures),[5,6] Blazer[1] concluded that somatic and emotional symptoms associated with depression present similarly across adulthood.

Over the past two decades, research has continued to examine whether phenomenological differences in depression emerge during older adulthood.[7–12] Age-based differences in depression is important to understand as variations in clinical presentations could contribute to misdiagnosis or incorrect treatment.[12,13] One approach to examining the phenomenology of depressive symptoms across adulthood is to compare depressive symptoms in younger and older adults diagnosed with MDD according to diagnostic criteria outlined in major classification systems (e.g., *Diagnostic and Statistical Manual for Mental Disorders*).[14] Hegeman et al.[7] conducted a meta-analysis of 11 studies that compared depressive symptoms endorsed by younger (aged <40 to 65 years) and older (aged 50–70 years) adults on the Hamilton Rating Scale for Depression,[15] a clinician-administered assessment of depressive symptomology. Among older adults, hypochondriasis, general and gastrointestinal somatic symptoms, and agitation were more commonly endorsed, whereas guilt and loss of interest in sex were less commonly endorsed. Although some symptomatic differences were identified across age groups, Hegeman et al.[7] acknowledged several methodological issues that limit possible conclusions. First, data on comorbid physical problems were typically not available and were therefore not adjusted. Comorbid physical problems could account for the elevated somatic symptoms among older adults. Similarly, age of onset and chronicity of depression were not accounted for, which could influence the clinical presentation of depression. A large proportion of

participants were severely-depressed inpatients, which limits the generalizability of results to community samples. When one study examining psychotic depression was removed,[16] differences between younger and older adults were no longer significant for general and gastrointestinal somatic symptoms and loss of interest in sex. Finally, hypochondriasis and general somatic symptoms were moderately heterogeneous, which indicates that results across studies were not consistent for these symptom categories.[17] These limitations temper the study's conclusion that depression in older adults is symptomatically different from younger adults.[8,12]

In a subsequent study, Hegeman et al.[9] examined baseline data from the Netherlands Study of Depression in Older Persons (NESDO),[18] a multisite cohort study. The effect of chronic somatic diseases and aging on depressive symptoms were evaluated in depressed (N = 300) and nondepressed (N = 129) older adults. Depressive symptoms were assessed using the Inventory of Depressive Symptomatology-Self Report.[19] Participants were classified by age (age ≤70 years = younger old, age ≥70 years = older old) and by number of chronic somatic diseases (0–1, ≥2). In the depressed group, more chronic somatic diseases were associated with more severe somatic symptoms. Older age showed a trend toward less severe somatic symptoms ($p = 0.145$). In the nondepressed group, individuals with more chronic somatic diseases showed a trend toward more severe somatic symptoms ($p = 0.065$) and older age was associated with more severe somatic symptoms. These results suggest that older age and chronic somatic diseases are not uniquely related to elevated somatic symptoms in depression. Hegeman et al.[9] contend that the severity of depressive symptoms may be overestimated in older adults because of comorbid physical problems and underestimated in the oldest old because of a tendency to under-report depressive symptoms.

Additional studies that have examined symptomatic age differences in depression have arrived at inconsistent conclusions,[8,10–12] likely attributable to methodological reasons (e.g., variability in sample characteristics, confounding variables, and cross-sectional design). Schaakxs et al.[8] used data from the Netherlands Study of Depression and Anxiety (NESDA) and the NESDO to compare depressive symptoms among younger (N = 1,026; age 18–59 years) and older (N = 378; age ≥60 years) adults with MDD on the Inventory of Depressive Symptomatology-Self Report.[19] Older age was positively associated with the somatic/vegetative cluster of symptoms, including early morning waking, loss of interest in sex, sleep problems, psychomotor retardation, other bodily symptoms, and aches and pains ($B = 0.23$, $p < 0.001$). Although some cognitive symptoms (e.g., pessimism about the future) and mood (e.g., reduced pleasure or enjoyment) were associated with older age, the cognitive ($B = -0.04$, $p < 0.004$) and mood ($B = -0.20$, $p < 0.001$) clusters of symptoms were negatively associated with older age. Results remained after adjusting for number of chronic diseases. Schaakxs et al.[8] suggest that elevated somatic/vegetative symptoms in the elderly could explain why late-life depression is underdiagnosed.[20]

A recent retrospective study examined the relationship between core depressive symptoms and age. Wilkowska-Chmielewska et al.[10] reviewed records of younger (N = 130; age <44 years), middle-aged (N = 241; age 45–64 years), and older (N = 149; age >64 years) adult inpatients diagnosed with a depressive episode to investigate if depressive symptoms differed by age of hospitalization. Insomnia, difficulty falling asleep, decreased appetite and body weight, and memory impairment were more common in older adults. Complaints of somatic symptoms and hypochondriasis increased with age. The retrospective design did not allow for information regarding other psychiatric diagnoses or health status to be examined or controlled. Although some depressive symptoms were more common in the elderly, the authors concluded that age did not have an impact on the core symptoms of depression (e.g., depressed mood, psychomotor retardation, diminished energy, difficulty concentrating, and difficulty making a decision) required for diagnosis.

An alternative approach to examine whether depression is symptomatically different in older adulthood is to compare depressive symptoms in older adults with early versus late onset MDD. This method examines differences in depressive symptoms according to timing of the first depressive episode rather than current age, which avoids confounding older age with greater likelihood of having more depressive episodes during their lifetime.[12,13] Wilkowska-Chmielewska et al.[10] reviewed records of adult inpatients with early (N = 33; age <44 years), mid (N = 52; age 45–64) years, and late onset (N = 28; age >65 years) of a depressive

episode. A late-onset depressive episode was associated with increased somatic complaints and decreased activity compared with early-onset depressive episodes and increased interpersonal sensitivity compared with early-onset and mid-onset depressive episodes. The authors concluded that age of onset does result in some (nevertheless few) phenomenological differences.

Alvarez et al.[11] examined differences in depressive symptoms reported by adult inpatients who were divided into groups based on their current age (18–60 or >60 years) and whether they had early-onset (N = 31; age <60 years) or late-onset (N = 30; age >60 years) MDD with melancholia, with or without psychotic features. Although symptomatic differences across groups were not found for the HDRS,[15] the Hamilton Anxiety Scale,[21] or the Widlöcher Depression Retardation Scale,[22] older adults with late-onset depression reported lower anger and irritability on the Schedule for Affective Disorders and Schizophrenia.[23] Although this was a single, cross-sectional study with a small sample size, the homogeneous sample does suggest that the symptoms of melancholic depression generally tend to present similarly regardless of the age at which the disorder develops.

Grayson and Thomas[12] conducted a systematic review of 14 studies that compared depressive symptoms among older adults with early (N = 23,745; age <50 to 60 years) and late-onset (N = 11,191; age >60 to 65 years) MDD. One of the reviewed studies found that hypochondriasis, somatic delusions, and gastrointestinal symptoms were more common in late-onset depression,[24] but this association was not consistently found across studies. Depressive symptoms were more severe in late-onset depression; this finding might be because participants were severely depressed inpatients, however. Large-scale epidemiological studies have found that depressive symptoms are typically less severe in older adults than younger adults,[25] which suggests that severely depressed inpatients may not be the most representative sample. Consequently, the authors concluded that depressive symptoms did not significantly differ in older adults with early-onset versus late-onset MDD.

Although the literature has identified some age-related symptom discrepancies in depressive disorders, findings have generally been inconsistent across studies. Some cohort studies found that older adults endorsed elevated levels of somatic symptoms,[7,8] whereas another cohort study failed to find such differences.[9] Other work has found some symptomatic differences based on age of onset, although the authors suggested that these difference were not clinically meaningful to the diagnosis of depression.[10–12] There are some data to suggest that somatic symptoms may be more prevalent in older adults,[7,8,10–12] although only Schaakxs et al.[8] found this result after adjusting for the presence of chronic diseases.

Compared with the studies reviewed by Blazer[1] 20 years ago, the current literature has advanced, and includes findings that reflect diverse samples of older adults. Despite this substantial increase in research investigating the phenomenological differences of depressive symptoms across adulthood, a clear and consistent message has not yet emerged. There is currently insufficient empirical evidence available to conclude that phenomenological differences that have an impact on clinical diagnostic decision-making for depression exist among younger and older adults.[26]

Future research should aim to overcome several methodological limitations associated with the current literature. For example, only a limited number of the studies reviewed recruited samples including the oldest old, or individuals over the age of 85 years. Although these samples may be more challenging to recruit for because of physical and cognitive limitations and social and cultural barriers,[27] it is important investigate depressive symptoms across the entire lifespan. In addition, a significant portion of the studies reviewed focused on severely depressed inpatients rather than community samples that may be more representative of the population. Only one of the studies reviewed controlled for comorbid physical illness, which is a major confounding factor. Depression in older adulthood is associated with increased rates of medical comorbidities.[28] More high-quality research that evaluates current symptoms, comorbid physical illnesses, depressive symptom severity, age of onset, and chronicity of depression at multiple time points is needed to assess if systematic differences in the presentation of depression exist across age groups and if these differences are clinically meaningful.

Finally, our understanding of the phenomenology of depression in older adulthood has been constrained by the research community's reliance on diagnostic criteria outlined in the *Diagnostic and Statistical Manual for Mental Disorders* (DSM).[14] The DSM-5 states that depressive symptomatology differ across the lifespan; however, with the exception of permitting "irritable

mood" to substitute for depressed mood in children and adolescents, criterion symptoms are assigned similarly across the lifespan. Reliance on the DSM categorical approach likely obscures heterogeneity and possible age-related depressive subtypes. For example, a DSM diagnosis of depression requires that an individual experience depressed mood and/or loss of interest or pleasure, which may be problematic given longitudinal research that suggests that older adults are less likely to endorse sadness.[29] If distinctive features of depression in older adulthood exist, it is likely that older adults with "non–DSM-defined depression" are not represented in research that compares symptom profiles. Similarly problematic is the DSM-5 requirement that comorbid symptoms be recently exacerbated in order to count toward a diagnosis of depression. This may differentially impact older adults who are more likely to have comorbid medical problems and fail to accurately attribute symptoms to MDD.

MYTH 2: DEPRESSION IS MORE COMMON IN LATE LIFE THAN AT YOUNGER AGES

Aging is associated with unique challenges including changes in independence, financial status, interpersonal relationships, and physical and cognitive abilities. In light of these challenges, it is often assumed that MDD in older adulthood is more prevalent than at younger ages. Blazer[1] reviewed evidence, including results from large epidemiological studies of community samples, on the prevalence rates of clinical depression in older adults ranging from 0.6% to 2%, which were significantly lower than estimates for younger adults.

In line with prior findings, the notion that older adults experience elevated levels of depression continues to remain a myth. Although older adults experience clinically significant depressive symptoms (8%–16% estimated prevalence rate)[30] and subclinical depression (10%–50% estimated prevalence rate depending on setting),[31] the literature has consistently shown that the prevalence and incidence rates for the clinical diagnosis of MDD in older adults is significantly lower than younger and middle-aged adults.

The prevalence rate (i.e., proportion of the population who have a condition during a specific period of time) of depression in older adults has been investigated for the past six decades. Beekman et al.[32] completed a systematic review of to assess the worldwide prevalence rate of depressive disorders in older adults (age >55 years). Prevalence rates varied when assessing for the presence of any clinically significant depressive symptoms, ranging from 2.4% in Japan to 35% in China. Prevalence rates were more consistent, however, when studies specifically assessed for MDD. The prevalence of MDD ranged from 0.4% in Japan to 10.2% in Australia, which was the only study that reported a prevalence rate above 5%. Excluding this study, the weighted average prevalence rate for the remaining 16 studies was 1.77%.

Recent reports of prevalence rates for MDD conclude that the disorder occurs less frequently in older adults. Although community-based samples of older adults above the age of 55 or 65 years report 12-month prevalence rates ranging as high as 4%[33–35] and 8.7%,[36] respectively, the majority of studies report prevalence rates at or below 2.6%.[25,37–44] Despite different prevalence rates, the aforementioned studies found that older participants had a lower prevalence of MDD compared with younger and middle-aged counterparts in the sample as well as most recent estimates of prevalence rates for younger (10.4% 1-year prevalence rate) and middle-aged (7.7–9.4% 1-year prevalence rate) adults.[25] There is no support for the claim that compared with younger adults, MDD is more prevalent in community-dwelling older adults.

A subset of older adults reside in long-term care facilities such as nursing homes, assisted living facilities, continuing care retirement communities, hospice care, and home care. In 2011, just 6.4% of older adults (age ≥65 years) in the United States were receiving long-term care.[45] Systematic reviews report prevalence rates of MDD that range from 5% to 25% in these settings,[46,47] with a median prevalence rate of 10%.[46] The prevalence of depression is higher in older adults living in long-term care facilities compared with those living in the community, although it is only slightly higher than middle-aged adults and comparable to younger adults.[25]

Although prevalence rates are more commonly reported, they can be greatly influenced by the chronicity of a disorder.[48] This is an important issue, because depression is marked by elevated rates of relapse and recurrence. Incidence rates (i.e., number of new cases in a given time period) may provide a better measure of the association between depression and aging as they

account for chronicity. Incidence rates for the first onset of depression have generally been lower in older adults compared with younger (1.9% 1-year incidence rate, 3.2 per 1,000 risk-years) and middle-aged (1.6% 1-year incidence rate, 1.9–5.4 per 1,000 risk-years) adults.[37,49] Community-based studies completed in the United States that report percentages range from 1.2% 1-year incidence rate for individuals over the age of 55 years[49] to 3.28% 3-year incidence rate for individuals over the age of 60 years.[50] Older adults who receive long-term care have slightly higher rates that range from 4.7% 6-month incidence rate[51] to 6.4% 1-year incidence rate.[52]

Community-based studies that have reported person-time incidence rates (i.e., number of new cases that occur within the amount of time that the sample was at risk for developing the disease of interest) report a greater range of incidence values depending on the study's parameters. Eaton et al.[37] obtained the lowest incidence rate using the Diagnostic Interview Schedule.[53] Over the course of 23 years, incidence rates for older adults from the United States over the age of 65 years reduced from 0.9 per 1,000 person-years between 1981 and 1993 to 0 per 1,000 person-years between 1993 and 2004. Murphy et al.[54] found a steady incidence rate in two cohorts from Canada using the DePression and AnXiety (DAPX) interview.[55] The incidence rates for older adults over the age of 55 years was 4.7 per 1,000 person-years between 1952 and 1970 and 3.9 per 1,000 person years between 1970 and 1992, yielding a combined incidence rate of 4.5 per 1,000 person-years. Using a semi-structured psychiatric interview, Luijendijk et al.[56] found that the incidence rate for MDD and dysthymia was 2.1 per 1,000 person-years in older adults (age ≥55 years) from the Netherlands. Norton et al.[57] found that the incidence rate for MDD was 10.51 per 1,000 risk-years in older adults from the United States aged 65 to 100 years. This rate is relatively higher than other studies, possibly because MDD was assessed using multiple approaches beyond a structured interview, including antidepressant use and postmortem informant interviews. Although incidence rates generally decreased over time, there were no significant differences when comparing age groups.

Although incidence rates of depression generally appear lower for older adults compared with younger and middle-aged adults, it is important to note that higher incidence rates have been found when assessing for the new onset of depressive disorders other than MDD such as dysthymia, minor depression, and MDD not otherwise specified (MDD-NOS). Luijendijk et al.[56] obtained a relatively low incidence rate of 7.0 per 1,000 person-years, which remained stable when examining incidence rates for depressive disorders across age groups. Norton et al.[57] found an incidence rate of 23.5 per 1,000 risk-years. Relative risks for developing a depressive disorder (i.e., MDD, subclinical depression, bereavement, dysthymia, and dysphoria) did not significantly differ between age groups.

Conversely, Palsson et al.[48] found significantly greater incidence rates for depressive disorders (i.e., MDD, dysthymia, and MDD-NOS) that increased with age in a Swedish cohort. The overall incidence rate for participants aged 70 to 85 years was 22.6 per 1,000 person-years. When comparing age groups, incidence rates appeared to increase with every age increment, peaking at 59.9 per 1,000 person-years for participants aged 81 to 83 years. The elevated rates reported in this study likely reflect the impact of dysthymia, which was the most frequently made diagnosis during the follow-up period.

The empirical evidence continues to find that older adults report lower prevalence and incidence rates of MDD than younger counterparts. Although older adults are less likely to experience MDD than younger adults, higher incidence rates of other depressive disorders (i.e., dysthymia, minor depression, MDD-NOS) have been reported and have important clinical implications. Older adults with clinically significant depressive symptoms or subthreshold depressive syndromes report levels of impairment in physical, social, and role functioning similar to MDD.[58] This finding has significant clinical relevance and underscores the importance that healthcare providers are able to detect and aggressively treat subclinical depressive syndromes in older adults.

MYTH 3: DEPRESSION IS MORE CHRONIC IN LATE LIFE THAN IN YOUNGER PERSONS

Depression in older adulthood is often associated with known prognostic factors, such as physical illness, cognitive impairment, and lack of social support, which makes it reasonable to speculate that depression during this period is more chronic or prone to relapse. Twenty years ago, Blazer[1] conducted a review of several

longitudinal studies[59–61] and concluded that the course of depression among older adults was similar to that among younger adults. The relationship between the course of depression and age is complex and few methodologically rigorous studies have conducted direct comparisons between middle-aged and older adults.[10]

To clarify the prognosis of depression among older adults, Mitchell and Subramaniam[13] conducted a systematic review to compare relapse and recurrence of depression in older adulthood to those with depression in middle adulthood. Studies were included if they compared depression in late life with depression in midlife. Regarding relapse and recurrence, one inception cohort design that examined the effect of randomized maintenance treatment on relapse to depression in patients older than 59 years of age was identified.[62] Participants received acute treatment (i.e., combination of nortriptyline and interpersonal psychotherapy) followed by randomized maintenance treatment (i.e., nortriptyline, interpersonal psychotherapy, or placebo) to prevent recurrence. Higher age at study entry was associated with greater relapse such that patients aged 70 years and older had a higher and quicker rate of recurrence than those aged 60 to 69 years. Although the authors did not specifically control for clinical variables that have been previously associated with greater relapse (e.g., number of previous episodes, age at index depressive episode, and medical comorbidity), analyses showed that none of these factors predicted relapse.[62]

The National Institute for Mental Health Collaborative Depression Study utilized a large-scale 15-year prospective design to examine time until recurrence in participants (age 17–30, 31–50, 51–64, and 65–79 years) who had recovered from depression.[63] The median time to recovery was similar across groups; the median time to recurrence, however, was shortest for the oldest participant group (age 65–79 years). This finding might be because older adults were more likely to have greater number of past episodes, because inclusion criteria required that all participants have a diagnosis of recurrent depression.

More recently, data from the NESDO was used to examine the course and outcomes of depressive disorders in adults over 60 years of age.[64] A total of 378 depressed patients (i.e., DSM-defined MDD, dysthymia, or minor depression) from specialized mental health facilities and 132 nondepressed adults participated in assessments every 6 months during the 2-year follow-up period. Of the 285 persons who were depressed at baseline, almost half (48.4%) also suffered from a depressive disorder 2 years later. Only 19% of individuals who were depressed at baseline were in complete remission. Almost two-thirds (61%) of depressed individuals at baseline had a chronic course, and 20% had an intermittent course (i.e., one assessment period without depressive symptoms). Results were compared with results from NESDA,[65] a similarly designed longitudinal study that examined relapse to depression among adults aged 18 to 65 years. In that study, about 80% of the purely depressed patients reached remission within 2 years, and only 50% of those with a comorbid anxiety disorder reached remission. In the NESDO study, only 36.8% of the depressed persons had a comorbid anxiety disorder; nevertheless, comorbidity was not a predictor of depressive diagnosis at follow-up. Comijis et al.[64] concluded that their results confirm the poorer prognosis of depression in terms of chronicity among older adults. Several determinants of the poor prognosis were identified and included baseline severity of depression, comorbid dysthymia, younger age of onset, and presence of chronic diseases.

As participants in the NESDO study were recruited from specialized mental health facilities, findings may not be generalizable to community-dwelling older adults. A recent systematic review examined the prognosis of depression in older adults (age ≥55 years) in general practice and the community.[66] Studies were included if they enrolled patients with clinically significant symptoms of depression or a depressive disorder diagnosis and provided at least one follow-up assessment. Regardless of the follow-up period or how depression was defined at baseline, results revealed that 20% to 50% of patients developed a chronic course.

In comparison, the Netherlands Mental Health Survey and Incidence Study (NEMESIS) provided data on the course of depression in the general population aged 18 to 64 years.[67] The NEMESIS study is a prospective, psychiatric epidemiological survey conducted in the Dutch adult general population with three waves (1996, 1997, and 1999). A total of 4,796 respondents participated in structured clinical interviews at all three waves. The study identified new episodes of major depression (N = 273) by including participants who endorsed a diagnosis of MDD at time 2 but denied a diagnosis of MDD at time 1. Results revealed that 76% of patients with depression recovered within 12

months. Determinants of persistence were severity of depression and comorbid dysthymia.

When Licht-Strunk et al.[66] assessed studies that allowed for examination of course (i.e., designs with more than two measurements), they found that about one-third of depressed older adults (≥55 years) developed a chronic course and another third had a brief period of remission. Evidence for a strong association between prognostic factors and poor outcome were found for higher age, chronic somatic comorbidity, greater functional impairment, higher baseline depression, and external locus of control.

Findings from the systematic review[13] and more recent longitudinal studies[64,66] support the notion that depression in older adulthood is associated with a worse trajectory—likely moderated by depression severity, number of previous episodes, and medical comorbidity. Licht-Strunk et al.[66] found strong evidence that older age, presence of chronic somatic diseases, higher baseline depression level, and an external locus of control were associated with poor outcome in two high-quality cohort studies. Similarly, Comijis et al.[64] found that patients with more severe depression at baseline, comorbid dysthymia, younger age of onset, and chronic physical diseases were more likely to have a poor outcome at 2-year follow-up.

MYTH 4: DEPRESSION IN LATE LIFE IS MORE DIFFICULT TO TREAT THAN DEPRESSION AT YOUNGER AGES

Reduced confidence in treatment efficacy for depression in older adults may contribute to delayed referral and treatment-seeking.[68] Fortunately, a large body of literature supports the efficacy of treatment for depression including psychotherapy, pharmacotherapy, and electroconvulsive therapy (ECT) for older adults. A recent meta-analysis found that psychological treatments of depression in older adults have a moderate to high effect on depression that were durable for at least 6 months.[69] Subgroup analyses confirmed the effectiveness of cognitive behavior therapy (CBT), life-review therapy, and problem-solving therapy, although non-directive counseling was found to be less effective. Additional work supports these findings but notes that the magnitude of the effect depends on the type of control; specifically, that change associated with supportive therapy or placebo plus clinical management are considerable.[70]

An area that has received less attention is whether depression in late life is equally responsive to treatment than at younger ages. Although there is a paucity of research that directly compares the association between treatment outcome and age, a recent study examined the effectiveness of CBT for depression in older versus younger veterans.[71] A large number (N = 864) of older (N = 100) and younger (N = 764) highly depressed veterans received 12 to 16 sessions of CBT-Depression, a treatment protocol developed for veterans and military service members to treat depression. Both younger and older adults experienced significant equivalent reductions in depressive symptoms. The magnitude of the effect was identical for both groups (d = 1.01). Using a similar design, Karlin et al.[68] demonstrated equivalent effectiveness of acceptance and commitment therapy for depression in a sample of older and younger adults.

Using an alternative strategy to compare treatment efficacy, Cuijpers et al.[72] conducted a meta-regression analysis of 112 studies to examine the relative efficacy of psychotherapy for depression in younger and older age groups. A total of 7,845 depressed participants (N = 4,588 in the experimental group, N = 3,257 in the control group) were included in analysis. Results indicated that a variety of types of psychotherapy (i.e., CBT, problem-solving therapy, interpersonal psychotherapy, and behavioral activation) for depression appear to be as effective in older adults as younger adults.[72]

In recognition of the particularly chronic nature of depression in older adulthood, research has begun to examine the efficacy of interventions designed to target and reduce depressive relapse. Mindfulness-based cognitive therapy[73] is an effective therapy that aims help patients become aware of, and respond more effectively to, negative thinking patterns that otherwise increase vulnerability to depression.[74] High-quality studies are needed to bolster the emerging evidence for the efficacy of mindfulness-based cognitive therapy among older adults.[75–79]

Research also supports the efficacy of antidepressants compared with placebo for the treatment of MDD in older adults.[80–82] These largely positive findings are attenuated or indeterminate for certain subgroups of older adults (e.g., nursing home residents who are typically older, with more medical comorbidity, functional, and cognitive impairment).[83] There is also insufficient

evidence for the efficacy of antidepressants for older adults with depression and comorbid dementia.[84–86]

Although antidepressants are efficacious for community-dwelling older adults with depression, evidence suggests that this efficacy is reduced in comparison with younger adults.[87,88] Nelson et al.[87] conducted a meta-analysis of 10 acute-phase, double-blind, randomized, placebo-controlled trials of second-generation antidepressants for the treatment of depression among participants aged 60 years and older. Second-generation antidepressants were modestly more efficacious than placebo, although the response rate (44.4%) was lower than the reported response rates (53.8%) in a meta-regression for adults younger than 65 years.[89] The efficacy of both first- and second-generation antidepressants for the treatment of MDD in adults was further examined in a meta-analysis and meta-regression of placebo-controlled randomized trials.[88] Older adults (age ≥55 years) had significantly higher response rates to antidepressant therapy than placebo. Meta-regression analyses indicated that the rate of response to antidepressants was significantly higher among adults younger than 50 years compared with studies on older adults (age >65 years). Sub-analyses revealed that for older adults (age >65 years), antidepressants were no more effective than placebo. Results suggest that, although antidepressants for older adults are efficacious, the response rate may be lower than those reported for adult samples (i.e., age <65 years). Research should continue to consider moderators of lowered treatment response in older adults, including sociodemographic and clinical factors (e.g., male sex, older age, and longer duration of depressive episode),[90] and aspects of executive functioning.[91]

The use of other classes of medications, such as anticonvulsants and antipsychotics, in combination with antidepressants has been explored as second-line treatments for treatment-resistant depressed older adults. Support for lithium augmentation in treatment-resistant late-life depression exists; nevertheless, older adults have had poorer tolerance of this class of medication.[92,93] Therefore, the use of antipsychotics in this population has been explored. Lenze et al.[94] conducted a large, multisite double-blind placebo-controlled randomized clinical trial of aripiprazole augmentation in older adults with treatment-resistant depression. Older adults (age >60 years) had significantly higher remission rates with aripiprazole and antidepressant therapy than placebo—a finding that remained stable over the 12-week continuation period. Although promising, more research is needed on the efficacy, safety, and tolerability.

Beyond the acute treatment phase, risk of relapse and recurrence raise concerns about durability of antidepressants treatment response. A recent meta-analysis of eight double-blinded randomized controlled trials found support for continuation treatment with antidepressants (tricyclic and selective serotonin reuptake inhibitors) compared with placebo for MDD in older adults.[95] Despite this evidence, additional research is needed with longer follow-up periods[96] and to compare the efficacy of long-term treatment outcomes for older patients and between both age groups.

It is widely agreed that ECT is an efficacious treatment of depression in older adults.[97,98] Compared with antidepressant treatment, ECT is associated with a faster rate of remission.[99] Older adults, as compared with younger adults, may experience greater benefit, such as rapid remission[100] and lower re-hospitalization rates.[101] Data from a prospective randomized multicenter clinical trial found that patients older than 46 years had a superior treatment response compared with younger counterparts.[102] Moreover, the effect of age on depressive symptoms remained significant after adjustment for psychosis status, initial severity, and number of previous episodes. Additional prospective studies provide further support that older adults may experience a superior response to ECT compared with younger counterparts.[103]

In contrast, several retrospective studies have not provided support for older age as a clinical predictor of treatment response to ECT.[104–106] Birkenhager et al.[107] used a retrospective design to compare the efficacy of ECT for depression among older adults (>65) and younger adults (18–45 and 45–64 years). ECT was equally efficacious for all patients, such that age did not influence treatment response. Nonetheless, the authors speculated that the failure to find an effect for age was likely because of the small number of patients included in the 18- to 45-year-old group.[107] In a retrospective chart review study, Sphashett et al.[108] found that older age and despondency predicted ECT treatment outcome in the nonpsychotic depressed group. Similarly, older age alone predicted treatment response to ECT among individuals with depression with psychotic features. Overall, ECT is efficacious among older adults and older age is generally regarded as a favorable predictor of treatment response.[109] With respect to relapse and recurrence, research has examined the

efficacy of maintenance ECT. A recent systematic review suggests that, if following a fixed treatment schedule, maintenance ECT is comparable in efficacy to continuation psychopharmacology for this age group.[110]

Evidence clearly indicates that treatment of the acute phase of depression is not more difficult to treat in older adulthood than at earlier ages. With the exception of a possible reduced response to antidepressants, older adults do not differ from adults at earlier stages in life in terms of acute response to treatment. Nonetheless, given the increased likelihood of relapse and recurrence to depression among older adults, maintaining remission status represents a significant challenge, which requires close monitoring and possible maintenance treatment.

MYTH 5: DEPRESSION IN LATE LIFE IS MORE OFTEN CAUSED BY PSYCHOLOGICAL FACTORS

Too often, depression in late life is perceived as an expected psychological reaction to the challenges associated with aging. Older adults are commonly portrayed as depressed, lonely, and preoccupied by impending disability and death. This fosters the idea that older adulthood is an inherently depressogenic stage of life. Interestingly, among the many factors that contribute to late-life depression, psychological factors may actually be more protective in later stages of life.[111]

Older adults may benefit from several psychological and social factors that may protect against depressive disorders in later life compared with earlier stages in life.[111] Results from longitudinal studies have revealed that older age is related to increases in subjective well-being[112] and decreases in negative affect.[113] Blanchflower and Oswald[114] examined the relationship between age and well-being using combined data from 500,000 Americans and Europeans over more than three decades. Findings, which were robust against cohort effects and accounted for select confounding factors (e.g., income and marital status), revealed that subjective happiness and well-being follows a U-shape, with middle-adulthood being associated with the lowest levels.

Several theories have been offered to account for the finding that older adults report high levels of well-being.[115] The socioemotional selectivity theory suggests that self-regulation of emotional functioning is spared from age-related decline, if not enhanced.[116] According to this theory, older adults are more mindful of their finite existence and therefore motivated to pursue emotionally meaningful goals as they age.[117] The "positivity effect," or developmental shift among older adults to favor positive material, is thought to facilitate emotion regulation[117] and may be account for age-related differences in psychopathology.[115] An alternative theory proposes that adverse life events (e.g., death of a spouse) are considered "on time" events that commonly and expectedly occur during this stage of life. Older adults may be more likely to anticipate the occurrence of adverse events and rehearse the experience in their mind, which may lessen the psychological and emotional impact of the event.[111] Nonetheless, similar to other periods across the lifespan, stressful life events, which are more commonly bereavement, illness, or disability in older adulthood, interact with biological, social, and psychological vulnerability factors (e.g., degree of perceived control, helplessness, burdensomeness, and a ruminative coping style)[118] to predict depressive symptoms.[119,120] There is insufficient evidence to indicate that the impact of the stressor differs by age.[120]

In line with the equifinality of depression, several age-related biological processes significantly contribute to the incidence and recurrence of depression in older adulthood.[121,122] The three major etiological hypotheses that have been proposed[123] for understanding the biological mechanisms associated with depression in older adulthood are 1) the "vascular hypothesis," which implicates the involvement of white matter hyperintensities,[124] 2) the "inflammatory hypothesis," which suggests that depression is associated with age related increases in inflammation,[125] and 3) the "degenerative hypothesis," which suggests that depression is a prodromal marker of cognitive impairment and dementia.[126] These hypotheses are not mutually exclusive and likely implicate the overlapping role of inflammation.[123]

The vascular depression hypothesis maintains that cerebrovascular disease, including small vessel ischemic change, may predispose, precipitate, or perpetuate depressive symptoms in late life.[124,127,128] A large body of work suggests that vascular lesions in the deep white matter tracts disconnect prefrontal cortical regions from striatal and limbic areas and this disruption contributes to the development of depressive symptoms (see Rutherford et al.[122] for a review).

The inflammation hypothesis proposes that metabolic, rather than vascular, processes lead to changes

in the function of cognitive and emotion neural networks. Although inflammation is implicated in depression across the lifespan, aging and related disease processes may contribute etiologically to at least some of the depressive syndromes in late life by contributing to metabolic changes, or increasing abnormalities in brain structures relevant to depression.[125] Older adults are in a chronic state of neuroinflammation characterized by continuous production of proinflammatory cytokines (e.g., interleukins, colony-stimulating factor, and tumor necrosis factor-alpha). Neuroinflammation has been hypothesized to induce stress-reactive hormonal and brain neurotransmitter changes similar to those found in depression. Cytokines alter production, metabolism, and transport of neurotransmitters that synergistically affect neural activity in mood-relevant brain regions.[129] Cumulative data indicate that proinflammatory cytokines are associated with the future development of clinically significant depression among older adults.[129]

Neuroinflammation may also account for the relationship between depression and neurodegenerative diseases, such as Alzheimer disease. Indeed, depression may represent an early symptom, risk factor, or prodrome of dementia.[121,126] The exaggerated release of proinflammatory cytokines can lead to neuronal damage.[130] Specifically, increases in proinflammatory cytokines interfere with anti-inflammatory and immunosuppressant regulation, leading to cognitive impairments associated with neurodegeneration[123] and decreased neurogenesis in selected brain areas including the hippocampus,[131] where reduced hippocampal volume is one of the early brain changes associated with dementia.[132]

Advances in the field of geriatric psychiatry have confirmed that late life depression is a product of a complex interaction of biologic, psychological, and social factors.[121,133] Nonetheless, many continue to believe that depression in older adulthood is a normative aspect of achieving advanced age. Unfortunately for caregivers and older adults with depression, this mentality may impede treatment-seeking.

CONCLUSIONS

The goal of this special article was to provide a 20-year update on the status of five commonly believed myths about depression in older adulthood.[1] Results reveal that important advances have been made toward our understanding of depression in older adulthood. With respect to the belief that depression is symptomatically different in older adults, research continues to examine this question. Currently, there is some evidence that the phenomenology of depression differs in older adults compared with younger adults. More specifically, somatic symptoms may be more prevalent in the elderly and individuals with late-onset depression.[7,8,10–12] Nevertheless, there is not a preponderance of high-quality evidence to suggest that these symptomatic differences are either consistent across different samples or clinically meaningful.[26] More-sophisticated research with careful symptom assessment is needed clarify the influence of comorbid medical condition and aging on depression.

In line with findings from 20 years ago, MDD in older adulthood remains less common in younger and middle adulthood. Twelve-month prevalence rates for MDD in older adults range from 0.3% to 10.2% compared with the most recent estimates of 10.4% in younger adults and 7.7% to 9.4% in middle-aged adults.[25] The person-time incidence rates range between 0 and 10.51 per 1,000 risk-years compared with available estimates of 3.2 per 1,000 risk-years in younger adults and 1.9–5.4 per 1,000 risk-years in middle-aged adults.[37] Importantly, others have argued that the presence of subclinical levels of depressive symptoms, which are more prevalent in the elderly (10%–50% prevalence in older adults compared with 14.22%–15.96% prevalence in younger and middle-aged adults),[134] have a significant impact on functioning and warrants clinical intervention.

Although prevalence and incidence rates do not differ based on age, this does not appear to be the case regarding the course of depression. Older adults with a history of MDD have a greater likelihood of experiencing a recurrence in older adulthood. Results of a systematic review[13] and findings from more recent longitudinal studies[65,66] indicate that depression in older adulthood is associated with a worse trajectory that is likely is moderated by depression severity, number of previous episodes, and medical comorbidity. Frequent relapse and recurrence associated with increased mortality underscore the looming public health implications of depression in older adulthood.

Efforts to evaluate interventions for depression in older adults has continued throughout the past 20 years. Evidence suggests that various types of psychotherapy are

equally effective for adults, both older and younger.[68,71,72] Despite reported efficacy of antidepressants for MDD in community-dwelling older adults, there is evidence to suggest that the response rate is lower compared with adults aged 65 years and younger.[87,88] Moreover, certain subgroups of older adults (e.g., nursing home residents, comorbid dementia patients, and treatment-resistant patients) are more challenging to treat. Research supports the efficacy of electroconvulsive therapy in the treatment of depression in older adults. Results from a randomized multicenter clinical trial[102] indicate that older adults may have a superior response to ECT than younger adults. Although some retrospective studies have not found a superior response to ECT among older adults, age is generally regarded as a favorable predictor of response to ECT.[108]

Finally, significant advances in our understanding of the link between depression and several age-related pathophysiological processes (i.e., cardiovascular, neuroanatomical, endocrine, and inflammatory or immune)[121–125] strongly refute the belief that that depression in older adulthood is primarily due to psychological reasons. Similar to younger adults, older adults may experience depression as a result of an interaction between stressful life events and psychological vulnerability, although there is also evidence to suggest that older adulthood might be associated with the presence of protective psychological factors. Research suggests that older adults tend to shift focus toward more positive material and this may result in spared or enhanced emotion regulation.[117]

Despite important advances in our understanding and treatment of depression in older adults, late-life depression remains a serious public health issue associated with high levels of morbidity, mortality,[135–137] and health care costs that are 50% higher than for nondepressed older adults.[137] Moreover, despite the availability of effective assessment tools and treatments, older adults with depression are nonetheless underdiagnosed and undertreated.[138]

This article spans several issues central to depression and aging, yet there are several important areas that warrant more attention and should be prioritized moving forward. Efforts should be made to disentangle the complex relationship between age-related pathophysiological processes, medical comorbidity, and depression.[139] Relatedly, rigorous prospective longitudinal research is needed to clarify potential mechanisms that may account for the strong association between depression and risk for dementia.[126]

Prevention efforts should be supported as an alternative strategy for reducing the burden of depression in older adults.[140] Prevention of MDD is one of the grand challenges in global mental health and is particularly important for older adults.[141] Promising prevention interventions have targeted high-risk older adults, including those in nursing homes[142] as well as primary care patients with subthreshold symptoms,[143] with macular degeneration,[144] and following surgery for a hip fracture.[145] Successful prevention efforts will likely capitalize on their ability to identity risk algorithms for a variety of biological and behavioral vulnerability factors.[146]

Finally, to stem depression's pernicious course, older adults require tailored psychosocial interventions that target depression and comorbid physical illness and depressive relapse. Successful dissemination will require scalable intervention strategies that harness novel service delivery approaches (e.g., peer support workers and Web-based telehealth) to target mental health disparities among older adults.[147]

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References

1. Blazer DG: Depression in the elderly. Myths and misconceptions. Psychiatr Clin North Am 1997; 20:111–119
2. Zarit SH, Orrell M: Special section on depression honoring emeritus editor Dan G. Blazer. Aging Ment Health 2014; 18:537
3. Blazer DG, Bachar JR, Highes DC: Major depression with melancholia: a comparison of middle-aged and elderly adults. J Am Geriatr Soc 1987; 35:927–932
4. Radloff LS: The CES-D scale: a self-report depression scale for research in the general population. Appl Psychol Meas 1977; 1:385–401
5. Berkman LF, Berkman CS, Kasl S, et al: Depressive symptoms in relation to physical health and functioning in the elderly. Am J Epidemiol 1986; 124:372–388
6. Ross CE, Mirowsky J: Components of depressed mood in married men and women: the center for epidemiologic studies depression scale. Am J Epidemiol 1984; 119:997–1004
7. Hegeman JM, Kok RM, van der Mast RC, et al: Phenomenology of depression in older compared with younger adults: meta-analysis. Br J Psychiatry 2012; 200:275–281
8. Schaakxs R, Comijs HC, Lamers F, et al: Age-related variability in the presentation of symptoms of major depressive disorder. Psychol Med 2016; 47:543–552
9. Hegeman JM, De waal MW, Comijs HC, et al: Depression in later life: a more somatic presentation? J Affect Disord 2015; 170:196–202

10. Wilkowska-Chmielewska J, Szelenberger W, Wojnar M: Age-dependent symptomatology of depression in hospitalized patients and its implications for DSM-5. J Affect Disord 2013; 150:142–145
11. Alvarez P, Urretavizcaya M, Benlloch L, et al: Early- and late-onset depression in the older: NO differences found within the melancholic subtype. Int J Geriatr Psychiatry 2011; 26:615–621
12. Grayson L, Thomas A: A systematic review comparing clinical features in early age at onset and late age at onset late-life depression. J Affect Disord 2013; 150:161–170
13. Mitchell AJ, Subramaniam H: Prognosis of depression in old age compared to middle age: a systematic review of comparative studies. Am J Psychiatry 2005; 162:1588–1601
14. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders. Fifth ed. Arlington, VA: American Psychiatric Publishing, 2013
15. Hamilton M: A rating scale for depression. J Neurol Neurosurg Psychiatry 1960; 23:56–62
16. Gournellis R, Oulis P, Rizos E, et al: Clinical correlates of age of onset in psychotic depression. Arch Gerontol Geriatr 2011; 52:94–98
17. Higgins JP, Thompson SG, Deeks JJ, et al: Measuring inconsistency in meta-analyses. BMJ 2003; 327:557–560
18. Comijs HC, Van Marwijk HW, Van der Mast RC, et al: The Netherlands study of depression in older persons (NESDO): a prospective cohort study. BMC Res Notes 2011; 4:524–534
19. Rush AJ, Gullion CM, Basco MR, et al: The inventory of depressive symptomatology (IDS): psychometric properties. Psychol Med 1996; 26:477–486
20. Mitchell AJ, Rao S, Vaze A: Do primary care physicians have particular difficulty identifying late-life depression? A meta-analysis stratified by age. Psychother Psychosom 2010; 79:285–294
21. Hamilton M: The assessment of anxiety states by rating. Br J Med Psychol 1959; 32:50–55
22. Widlöcher D: L'évaluation quantitative du ralentissement psychomoteur dans les états dépressifs. Psychol Med 1980; 12:2725–2739
23. Endicott J, Spitzer RL: A diagnostic interview: the schedule for affective disorders and schizophrenia. Arch Gen Psychiatry 1978; 35:773–779
24. Gallagher D, Mhaolain AN, Greene E, et al: Late life depression: a comparison of risk factors and symptoms according to age of onset in community dwelling older adults. Int J Geriatr Psychol 2010; 25:981–987
25. Kessler RC, Birnbaum H, Bromet E, et al: Age differences in major depression: results from the National Comorbidity Survey Replication (NCS-R). Psychol Med 2010; 40:225–237
26. Thomas A: Is depression really different in older people? Int Psychogeriatr 2013; 15:1739–1742
27. Mody L, Miller DK, McGloin JM, et al: Recruitment and retention of older adults in aging research. J Am Geriatr Soc 2008; 56:2340–2348
28. Ismail Z, Fischer C, McCall WV: What characterizes late-life depression? Psychiatr Clin North Am 2013; 36:483–496
29. Gallo JJ, Rabins PV, Anthony JC: Sadness in older persons: 13-year follow-up of a community sample in Baltimore, Maryland. Psychol Med 1999; 29:341–350
30. Blazer DG: Depression in late life: review and commentary. J Gerontol A Biol Sci Med Sci 2003; 58:249–265
31. Meeks TW, Vahia IV, Lavretsky H, et al: A tune in "a minor" can "b major": a review of epidemiology, illness course, and public health implications of subthreshold depression in older adults. J Affect Disord 2011; 129:126–142
32. Beekman AT, Copeland JR, Prince MJ: Review of community prevalence of depression in later life. Br J Psychiatry 1999; 174:307–311
33. Byers AL, Yaffe K, Covinsky KE, et al: High occurrence of mood and anxiety disorders among older adults: the National Comorbidity Survey Replication. Arch Gen Psychiatry 2010; 67:489–496
34. Mojtabai R, Olfson M: Major depression in community-dwelling middle-aged and older adults: prevalence and 2- and 4-year follow-up symptoms. Psychol Med 2004; 34:623–634
35. Steffens DC, Skoog I, Norton MC, et al: Prevalence of depression and its treatment in an elderly population: the Cache County Study. Arch Gen Psychiatry 2000; 57:601–607
36. McDougall FA, Kvaal K, Matthews FE, et al: Prevalence of depression in older people in England and Wales: the MRC CFA Study. Psychol Med 2007; 37:1787–1795
37. Eaton WW, Kalaydjian A, Scharfstein DO, et al: Prevalence and incidence of depressive disorder: the Baltimore ECA follow-up, 1981–2004. Acta Psychiatr Scand 2007; 116:182–188
38. Ford BC, Bullard KM, Taylor RJ, et al: Lifetime and 12-month prevalence of Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition disorders among older African Americans: findings from the National Survey of American Life. Am J Geriatr Psychiatry 2007; 15:652–659
39. Gum AM, King-Kallimanis B, Kohn R: Prevalence of mood, anxiety, and substance-abuse disorders for older Americans in the national comorbidity survey—replication. Am J Geriatr Psychiatry 2009; 17:769–781
40. Kessler RC, Berglund P, Demler O, et al: The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). JAMA 2003; 289:3095–3105
41. Narrow WE, Rae DS, Robins LN, et al: Revised prevalence estimates of mental disorders in the United States: using a clinical significance criterion to reconcile 2 surveys' estimates. Arch Gen Psychiatry 2002; 59:115–123
42. Pirkola SP1, Isometsä E, Suvisaari J, et al: DSM-IV mood-, anxiety- and alcohol use disorders and their comorbidity in the Finnish general population—results from the Health 2000 Study. Soc Psychiatry Psychiatr Epidemiol 2005; 40:1–10
43. Trollor JN, Anderson TM, Sachdev PS, et al: Prevalence of mental disorders in the elderly: the Australian National Mental Health and Well-Being Survey. Am J Geriatr Psychiatry 2007; 15:455–466
44. Wells JE, Browne MA, Scott KM, et al: Prevalence, interference with life and severity of 12 month DSM-IV disorders in Te Rau Hinengaro: the New Zealand Mental Health Survey. Aust N Z J Psychiatry 2006; 40:845–854
45. He W, Goodkind D, Kowal P: An aging world: 2015. Int Pop Rep 2016; 95:1–165
46. Thakur M, Blazer DG: Depression in long-term care. J Am Med Dir Assoc 2008; 9:82–87
47. Seitz D, Purandare N, Conn D: Prevalence of psychiatric disorders among older adults in long-term care homes: a systematic review. Int Psychogeriatr 2010; 22:1025–1039
48. Palsson SP, Ostling S, Skoog I: The incidence of first-onset depression in a population followed from the age of 70 to 85. Psychol Med 2001; 31:1159–1168
49. Grant BF, Goldstein RB, Chou SP, et al: Sociodemographic and psychopathologic predictors of first incidence of DSM-IV substance use, mood and anxiety disorders: results from the Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions. Mol Psychiatry 2009; 14:1051–1066
50. Chou KL, Mackenzie CS, Liang K, et al: Three-year incidence and predictors of first-onset of DSM-IV mood, anxiety, and substance

use disorders in older adults: results from Wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions. J Clin Psychiatry 2011; 72:144–155
51. Smalbrugge M, Jongenelis L, Pot AM, et al: Incidence and outcome of depressive symptoms in nursing home patients in the Netherlands. Am J Geriatr Psychiatry 2006; 14:1069–1076
52. Payne JL, Sheppard JE, Steinberg M, et al: Incidence, prevalence, and outcomes of depression in residents of a long-term care facility with dementia. Int J Geriatr Psychiatry 2002; 17:247–253
53. Robins LN, Helzer JE, Croughan J, et al: National Institute of Mental Health diagnostic interview schedule. Its history, characteristics, and validity. Arch Gen Psychiatry 1981; 38:381–389
54. Murphy JM, Laird NM, Monson RR, et al: Incidence of depression in the Stirling County Study: historical and comparative perspectives. Psychol Med 2000; 30:505–514
55. Murphy JM, Olivier DC, Monson RR, et al: Incidence of depression and anxiety: the Stirling County Study. Am J Public Health 1988; 78:534–540
56. Luijendijk HJ, Van den berg JF, Dekker MJ, et al: Incidence and recurrence of late-life depression. Arch Gen Psychiatry 2008; 65:1394–1401
57. Norton MC1, Skoog I, Toone L, et al: Three-year incidence of first-onset depressive syndrome in a population sample of older adults: the Cache County study. Am J Geriatr Psychiatry 2006; 14:237–245
58. Beekman AT, Geerlings SW, Deeg DJ, et al: The natural history of late-life depression: a 6-year prospective study in the community. Arch Gen Psychiatry 2002; 59:605–611
59. Keller MB, Shapiro RW, Lavori PW, et al: Recovery in major depressive disorder: analysis with the life table and regression models. Arch Gen Psychiatry 1982; 39:905–910
60. Murphy E: The prognosis of depression in old age. Br J Psychiatry 1983; 142:111–119
61. Baldwin RC, Jolley DJ: The prognosis of depression in old age. Br J Psychiatry 1986; 149:574–583
62. Reynolds CR III, Frank E, Perel JM, et al: Nortriptyline and interpersonal psychotherapy as maintenance therapies for recurrent major depression: a randomized controlled trial in patients older than 59 years. JAMA 1999; 281:39–45
63. Mueller TI, Kohn R, Leventhal N, et al: The course of depression in elderly patients. Am J Geriatr Psychiatry 2004; 12:22–29
64. Comijs HC, Nieuwesteeg J, Kok R, et al: The two-year course of late-life depression; Results from the Netherlands study of depression in older persons. BMC Psychiatry 2015; 15:20–29
65. Penninx BW, Nolen WA, Lamers F, et al: Two-year course of depressive and anxiety disorders: results from the Netherlands Study of Depression and Anxiety (NESDA). J Affect Disord 2011; 133:76–85
66. Licht-Strunk E, van der Windt DA, van Marwijk HW, et al: The prognosis of depression in older patients in general practice and the community. A systematic review. Fam Pract 2007; 24:168–180
67. Spijker J, De graaf R, Bijl RV, et al: Duration of major depressive episodes in the general population: results from The Netherlands Mental Health Survey and Incidence Study (NEMESIS). Br J Psychiatry 2002; 181:208–213
68. Karlin BE, Walser RD, Yesavage J, et al: Effectiveness of acceptance and commitment therapy for depression: comparison among older and younger veterans. Aging Ment Health 2013; 17:555–563
69. Cuijpers P, Karyotaki E, Pot AM, et al: Managing depression in older age: psychological interventions. Maturitas 2014; 79:160–169
70. Huang AX, Delucchi K, Dunn LB, et al: A systematic review and meta-analysis of psychotherapy for late-life depression. Am J Geriatr Psychiatry 2015; 23:261–273
71. Karlin BE, Trockel M, Brown GK, et al: Comparison of the effectiveness of cognitive behavioral therapy for depression among older versus younger veterans: results of a national evaluation. J Gerontol B Psychol Sci Soc Sci 2015; 70:3–12
72. Cuijpers P, Van straten A, Smit F, et al: Is psychotherapy for depression equally effective in younger and older adults? A meta-regression analysis. Int Psychogeriatr 2009; 21:16–24
73. Segal ZV, Williams JMG, Teasdale JD: Mindfulness-Based Cognitive Therapy for Depression: A New Approach to Preventing Relapse. New York, NY: The Guilford Press, 2002
74. Ma SH, Teasdale JD: Mindfulness-based cognitive therapy for depression: replication and exploration of differential relapse prevention effects. J Consult Clin Psychol 2004; 72:31–40
75. Smith A, Graham L, Senthinathan S: Mindfulness-based cognitive therapy for recurring depression in older people: a qualitative study. Aging Ment Health 2007; 11:346–357
76. Splevins K, Smith A, Simpson J: Do improvements in emotional distress correlate with becoming more mindful? A study of older adults. Aging Ment Health 2009; 13:328–335
77. Foulk MA, Ingersoll-dayton B, Kavanagh J, et al: Mindfulness-based cognitive therapy with older adults: an exploratory study. J Gerontol Soc Work 2014; 57:498–520
78. Meeten F, Whiting S, Williams CM: An exploratory study of group mindfulness-based cognitive therapy for older people with depression. Mindfulness 2015; 6:467–474
79. Williams MC, Meeten F, Whiting S: "I had a sort of epiphany!" An exploratory study of group mindfulness-based cognitive therapy for older people with depression. Aging Ment Health 2016; 1:1–10
80. Taylor WD: Clinical practice. Depression in the elderly. N Engl J Med 2014; 371:1228–1236
81. Thorlund K, Druyts E, Wu P, et al: Comparative efficacy and safety of selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors in older adults: a network meta-analysis. J Am Geriatr Soc 2015; 63:1002–1009
82. Kok RM, Nolen WA, Heeren TJ: Efficacy of treatment in older depressed patients: a systematic review and meta-analysis of double-blind randomized controlled trials with antidepressants. J Affect Disord 2012; 141:103–115
83. Boyce RD, Hanlon JT, Karp JF, et al: A review of the effectiveness of antidepressant medications for depressed nursing home residents. J Am Med Dir Assoc 2012; 13:326–331
84. Bains J, Birks J, Dening T: Antidepressants for treating depression in dementia. Cochrane Database Syst Rev 2002; (4):CD003944
85. Nelson JC, Devanand DP: A systematic review and meta-analysis of placebo-controlled antidepressant studies in people with depression and dementia. J Am Geriatr Soc 2011; 59:577–585
86. Banerjee S, Hellier J, Dewey M, et al: Sertraline or mirtazapine for depression in dementia (HTA-SADD): a randomized, multicentre, double-blind, placebo-controlled trial. Lancet 2011; 30:403–411
87. Nelson JC, Delucchi K, Schneider LS: Efficacy of second generation antidepressants in late-life depression: a meta-analysis of the evidence. Am J Geriatr Psychiatry 2008; 16:558–567
88. Tedeschini E, Levkovitz Y, Iovieno N, et al: Efficacy of antidepressants for late-life depression: a meta-analysis and meta-regression of placebo-controlled randomized trials. J Clin Psychiatry 2011; 72:1660–1668
89. Papakostas GI, Fava M: Does the probability of receiving placebo influence clinical trial outcome? A meta-regression of double-blind, randomized clinical trials in MDD. Eur Neuropsychopharmacol 2009; 19:34–40

90. Calati R, Salvina Signorelli M, Balestri M, et al: Antidepressants in elderly: metaregression of double-blind, randomized clinical trials. J Affect Disord 2013; 147:1–8
91. Pimontel MA, Culang-reinlieb ME, Morimoto SS, et al: Executive dysfunction and treatment response in late-life depression. Int J Geriatr Psychiatry 2012; 27:893–899
92. Cooper C, Katona C, Lyketsos K, et al: A systematic review of treatments for refractory depression in older people. Am J Psychiatry 2011; 168:681–688
93. Maust DT, Oslin DW, Thase ME: Going beyond antidepressant monotherapy for incomplete response in nonpsychotic late-life depression: a critical review. Am J Geriatr Psychiatry 2013; 21:973–986
94. Lenze EJ, Mulsant BH, Blumberger DM, et al: Efficacy, safety, and tolerability of augmentation pharmacotherapy with aripiprazole for treatment-resistant depression in late life: a randomized placebo-controlled trial. Lancet 2015; 386:2404–2412
95. Kok RM, Heeren TJ, Nolen WA: Continuing treatment of depression in the elderly: a systematic review and meta-analysis of double-blind randomized controlled trials with antidepressants. Am J Geriatr Psychiatry 2011; 19:249–255
96. Diniz BS, Reynolds CF: Major depressive disorder in older adults: benefits and hazards of prolonged treatment. Drugs Aging 2014; 31:661–669
97. Damm J, Eser D, Schüle C, et al: Influence of age on effectiveness and tolerability of electroconvulsive therapy. J ECT 2010; 26:282–288
98. Dols A, Bouckaert F, Sienaert P, et al: Early- and late-onset depression in late life: a prospective study on clinical and structural brain characteristics and response to electroconvulsive therapy. Am J Geriatr Psychiatry 2017; 25:178–189
99. Spaans HP, Sienaert P, Bouckaert F, et al: Speed of remission in elderly patients with depression: electroconvulsive therapy v. medication. Br J Psychiatry 2015; 206:67–71
100. Rhebergen D, Huisman A, Bouckaert F, et al: Older age is associated with rapid remission of depression after electroconvulsive therapy: a latent class growth analysis. Am J Geriatr Psychiatry 2015; 23:274–282
101. Rosen BH, Kung S, Lapid MI: Effect of age on psychiatric rehospitalization rates after electroconvulsive therapy for patients with depression. J ECT 2016; 32:93–98
102. O'Connor MK, Knapp R, Husain M, et al: The influence of age on the response of major depression to electroconvulsive therapy: a C.O.R.E. report. Am J Geriatr Psychiatry 2001; 9:382–390
103. Wesson ML, Wilkinson AM, Anderson DN, et al: Does age predict the long-term outcome of depression treated with ECT? A prospective study of the long-term outcome of ECT-treated depression with respect to age. Int J Geriatr Psychiatry 1997; 12:45–51
104. Cattan RA, Barry PP, Mead G, et al: Electroconvulsive therapy in octogenarians. J Am Geriatr Soc 1990; 38:753–758
105. Burke WJ, Rubin EH, Zorumski CF, et al: The safety of ECT in geriatric psychiatry. J Am Geriatr Soc 1987; 35:516–521
106. Karlinsky H, Shulman KI: The clinical use of electroconvulsive therapy in old age. J Am Geriatr Soc 1984; 32:183–186
107. Birkenhäger TK, Pluijms EM, Ju MR, et al: Influence of age on the efficacy of electroconvulsive therapy in major depression: a retrospective study. J Affect Disord 2010; 126:257–261
108. Spashett R, Fernie G, Reid IC, et al: MADRS symptom subtypes in ECT-treated depressed patients: relationship to response and subsequent ECT. J ECT 2014; 30:227–231
109. Pinna M, Manchia M, Oppo R, et al: Clinical and biological predictors of response to electroconvulsive therapy (ECT): a review. Neurosci Lett 2016; doi:10.1016/j.neulet.2016.10.047
110. Van schaik AM, Comijs HC, Sonnenberg CM, et al: Efficacy and safety of continuation and maintenance electroconvulsive therapy in depressed elderly patients: a systematic review. Am J Geriatr Psychiatry 2012; 20:5–17
111. Blazer DG, Hybels CF: Origins of depression in later life. Psychol Med 2005; 35:1241–1252
112. Cacioppo JT, Hawkley LC, Kalil A, et al: Happiness and the invisible threads of social connection. In: Eid M, Larsen RJ, eds. The Science of Subjective Well-Being. New York, NY: The Guilford Press, 2008:195–219
113. Charles ST, Reynolds CA, Gatz M: Age-related differences and change in positive and negative affect over 23 years. J Pers Soc Psychol 2001; 80:136–151
114. Blanchflower DG, Oswald AJ: Is well-being U-shaped over the life cycle? Soc Sci Med 2008; 66:1733–1749
115. Urry HL, Gross JJ: Emotion regulation in older age. Curr Dir Psychol Sci 2010; 19:352–357
116. Charles ST, Carstensen LL: A life-span view of emotional functioning in adulthood and old age. In: Costa PT, Siegler IC, eds. Recent Advances in Psycholology and Aging. Vol. 15. New York, NY: Elsevier, 2004:133–162
117. Carstensen LL, Mikels JA: At the intersection of emotion and cognition aging and the positivity effect. Curr Dir Psychol Sci 2005; 14:117–121
118. Brinker JK: Rumination and reminiscence in older adults: implications for clinical practice. Eur J Ageing 2013; 10:223–227
119. Areán PA, Reynolds CF: The impact of psychosocial factors on late-life depression. Biol Psychiatry 2005; 58:277–282
120. Bruce ML: Psychosocial risk factors for depressive disorders in late life. Biol Psychiatry 2002; 52:1750184
121. Aziz R, Steffens DC: What are the causes of late-life depression? Psychiatr Clin North Am 2013; 36:497–516
122. Rutherford BR, Taylor WD, Brown PJ, et al: Biological aging and the future of geriatric psychiatry. J Gerontol A Biol Sci Med Sci 2016; 72:343–352
123. Martínez-Cengotitabengoa M, Carrascón L, O'Brien JT, et al: Peripheral inflammatory parameters in late-life depression: a systematic review. Int J Mol Sci 2016; 17:2022–2035
124. Alexopoulos GS, Meyers BS, Young RC, et al: "Vascular depression" hypothesis. Arch Gen Psychiatry 1997; 54:915–922
125. Alexopoulos GS, Morimoto SS: The inflammation hypothesis in geriatric depression. Int J Geriatr Psychiatry 2011; 26:1109–1118
126. Byers AL, Yaffe K: Depression and risk of developing dementia. Nat Rev Neurol 2011; 7:323–331
127. Alexopoulos GS, Meyers BS, Young RC, et al: Clinically defined vascular depression. Am J Psychiatry 1997; 154:562–565
128. Krishnan KR, Hays JC, Blazer DG: MRI-defined vascular depression. Am J Psychiatry 1997; 154:497–501
129. Kiecolt-Glaser JK, Derry HM, Fagundes CP: Inflammation: depression fans the flames and feasts on the heat. Am J Psychiatry 2015; 172:1075–1091
130. Hurley LL, Tizabi Y: Neuroinflammation, neurodegeneration, and depression. Neurotox Res 2013; 23:131–144
131. Maes M, Yirmyia R, Noraberg J, et al: The inflammatory & neurodegenerative (I&ND) hypothesis of depression: leads for future research and new drug developments in depression. Metab Brain Dis 2009; 24:27–53
132. Van de Pol LA, Hensel A, Barkhof F, et al: Hippocampal atrophy in Alzheimer disease: age matters. Neurology 2006; 66:236–238
133. Fiske A, Wetherell JL, Gatz M: Depression in older adults. Annu Rev Clin Psychol 2009; 5:363–389

134. Wittayanukorn S, Qian J, Hansen RA: Prevalence of depressive symptoms and predictors of treatment among U.S. adults from 2005 to 2010. Gen Hosp Psychiatry 2014; 36:330–336
135. Beekman AT, Deeg DJ, Braam AW, et al: Consequences of major and minor depression in later life: a study of disability, well-being and service utilization. Psychol Med 1997; 27:1397–1409
136. Unützer J, Patrick DL, Simon G, et al: Depressive symptoms and the cost of health services in HMO patients aged 65 years and older. A 4-year prospective study. JAMA 1997; 227:1618–1623
137. Katon WJ, Lin E, Russo J, et al: Increased medical costs of a population-based sample of depressed elderly patients. Arch Gen Psychiatry 2003; 60:897–903
138. Wang PS, Lane M, Olfson M, et al: Twelve-month use of mental health services in the United States: results from the National Comorbidity Survey Replication. Arch Gen Psychiatry 2005; 62:629–640
139. Morimoto SS, Alexopoulos GS: Cognitive deficits in geriatric depression: clinical correlates and implications for current and future treatment. Psychiatr Clin North Am 2013; 36:517–531
140. Cuijpers P, Smit F, Patel V, et al: Prevention of depressive disorders in older adults: an overview. Psych J 2015; 4:3–10
141. Reynolds CF III: Prevention of major depression: a global priority. In: Okereke OI, ed. Prevention of Late-Life Depression: Current Clinical Challenges and Priorities. New York, NY: Springer International Publishing, 2015:1–4
142. Konnert C, Dobson K, Stelmach L: The prevention of depression in nursing home residents: a randomized clinical trial of cognitive-behavioral therapy. Aging Ment Health 2009; 13:288–299
143. Van't veer-tazelaar PJ, Van marwijk HW, Van oppen P, et al: Stepped-care prevention of anxiety and depression in late life: a randomized controlled trial. Arch Gen Psychiatry 2009; 66:297–304
144. Rovner BW, Casten RJ, Hegel MT, et al: Preventing depression in age-related macular degeneration. Arch Gen Psychiatry 2007; 64:886–892
145. Burns A, Banerjee S, Morris J, et al: Treatment and prevention of depression after surgery for hip fracture in older people: randomized, controlled trials. J Am Geriatr Soc 2007; 55:75–80
146. Reynolds CF, Cuijpers P, Patel V, et al: Early intervention to reduce the global health and economic burden of major depression in older adults. Annu Rev Public Health 2012; 33:123–135
147. Bartels SJ, Pepin R, Gill LE: The paradox of scarcity in a land of plenty: meeting the needs of older adults with mental health and substance use disorders. Generations 2014; 38:6–13