

DEPRESSION AND COGNITIVE DECLINE

WHAT IS ALREADY KNOWN

Depression and dementia are prevalent and often co-occurring conditions among older adults, yet both are frequently under-recognized in clinical and community settings. While major depression becomes less common with age, milder and chronic depressive symptoms tend to increase in prevalence. Understanding the relationship between depression and dementia is important for informing early detection and care strategies. Depression may increase the risk of developing dementia, but it may also be an early indicator of neurodegenerative changes in the brain. In some cases, depressive symptoms may reflect the earliest manifestations of dementia-related pathology, rather than being a separate or preceding condition. Recognizing this complexity can help improve diagnostic accuracy, guide intervention timing, and shape more effective public health responses to aging-related cognitive decline.

BACKGROUND AND EVIDENCE BASE

Depression is a mood disorder that exists on a spectrum, from transient feelings of sadness to clinically diagnosed major depressive disorder (MDD), which is characterized by persistent low mood, loss of interest, and functional impairment. In research and clinical settings, depression is often measured using standardized diagnostic criteria or symptom scales, but definitions and severity thresholds can vary across studies. This variability is important to consider when interpreting the evidence linking depression and dementia.

Although much attention has focused on depressive “pseudodementia,” a classical presentation of impaired cognition due to underlying undiagnosed depression instead of neuropathology, decades of research have revealed that it is rare. Instead, depression may occur as an antecedent to dementia, including Alzheimer's disease. Both depression and anxiety have been shown to be associated with dementia and may be independent risk factors for Alzheimer's disease. However, there are discrepancies in the literature. In a study of over 500,000 military conscripts in Denmark, depression during adulthood was associated with increased risk of dementia later in life. In a 2021 longitudinal observational study, 16,608 people without prevalent dementia were followed for 6 years; depression in both adulthood and late life was associated with increased dementia risk, while depression occurring only in late life was associated with lower risk of

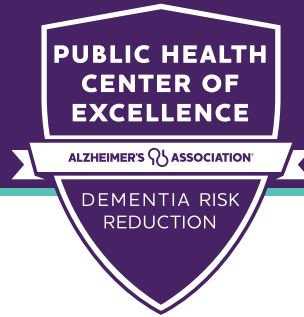
dementia. Resolution of adult-onset depression symptoms was not linked to a higher risk of developing dementia. In contrast, the longitudinal Swedish Twins Study (with over 40,000 participants) found that late-life depression was associated with a greater risk of Alzheimer's disease while mid- to late-life depression increased the risk of non-Alzheimer's disease subtypes of dementia that typically occur at younger ages.

Depression often presents as a coincident symptom in mild cognitive impairment (MCI), and its presence is associated with an increased likelihood of progression to Alzheimer's disease. There is also an association between depression and cerebrovascular disease in older adults that has led to the term “vascular depression.” In 443 Black participants enrolled in the National Alzheimer's Coordinating Center (NACC) dataset, depression and white matter hyperintensity volume were associated with a higher prevalence of dementia. In summary, there appears to be a bidirectional relationship between depression and Alzheimer's disease, including genetic predisposition, immune dysregulation, accumulation of Alzheimer's disease-related biomarkers (e.g., amyloid- β and tau), and alterations in brain structure including cerebrovascular disease.

There is less information and prospectively-collected data to address questions about depression and how its treatment earlier in life may affect cognition. This is largely because of the long time lag between diagnosis and treatment for depression, and cognitive decline or dementia later in life. The literature on whether depression in earlier life predicts the likelihood of developing dementia is mixed, with nearly all studies relying on history obtained from participants about decades-old depressive episodes because prospective evaluation over an entire lifetime is impractical. Similarly, data are limited on whether treatment of depression at younger ages may prevent cognitive decline and dementia in the distant future.

IMPLICATIONS FOR PUBLIC HEALTH

The association between depression and dementia highlights the need for proactive mental health strategies within public health systems. Early identification of depression may offer a critical window to reduce or delay cognitive decline. Public health initiatives should prioritize integrating depression screening into routine care for adults, particularly in midlife and older age, and ensure that treatment pathways are accessible and evidence-



based. While more research is needed to determine whether treating depression directly reduces dementia risk, the potential for long-term cognitive benefits reinforces the value of early intervention.

The role of social determinants of health

Social and environmental conditions play a significant role in shaping both depression and dementia risk. Individuals experiencing economic hardship, social isolation, or limited access to mental health care are more likely to have undiagnosed or untreated depression, which may contribute to accelerated cognitive decline. Structural barriers such as health care access, housing instability, and stigma around mental illness further complicate timely diagnosis and treatment. Addressing these upstream factors through community-based outreach, culturally responsive care, and cross-sector collaboration is essential to promoting mental and cognitive health across diverse aging populations.

DISCUSSION

Depression is closely linked to subsequent development of dementia, particularly Alzheimer's disease, vascular, and mixed dementia. Screening efforts for depression remain paramount in order to promote awareness and treatment. Early observational data suggests recovering from depression may be associated with bringing risk of subsequent dementia back down, but further research is needed to determine whether management of depression reduces dementia risk.

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