Depressive Symptoms in Middle Age and the Development of Later-Life Functional Limitations: The Long-Term Effect of Depressive Symptoms

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OBJECTIVES: To determine whether middle-aged persons with depressive symptoms are at higher risk for developing activity of daily living (ADL) and mobility limitations as they advance into older age than those without.

DESIGN: Prospective cohort study.

SETTING: The Health and Retirement Study (HRS), a nationally representative sample of people aged 50 to 61.

PARTICIPANTS: Seven thousand two hundred seven community living participants in the 1992 wave of the HRS.

MEASUREMENTS: Depressive symptoms were measured using the 11-item Center for Epidemiologic Studies Depression Scale (CES-D 11), with scores of 9 or more (out of 33) classified as significant depressive symptoms. Difficulty with five ADLs and basic mobility tasks (walking several blocks or up one flight of stairs) was measured every 2 years through 2006. The primary outcome was persistent difficulty with ADLs or mobility, defined as difficulty in two consecutive waves.

RESULTS: Eight hundred eighty-seven (12%) subjects scored 9 or higher on the CES-D 11 and were classified as having significant depressive symptoms. Over 12 years of follow-up, subjects with depressive symptoms were more likely to reach the primary outcome measure of persistent difficulty with mobility or ADL function (45% vs 23%, Cox hazard ratio (HR) = 2.33, 95% confidence interval (CI) = 2.06–2.63). After adjusting for age, sex, measures of socioeconomic status, comorbid conditions, high body mass index, smoking, exercise, difficulty jogging 1 mile, and difficulty climbing several flights of stairs, the risk was attenuated but still statistically significant (Cox HR = 1.44, 95% CI = 1.25–1.66).

CONCLUSION: Depressive symptoms independently predict the development of persistent limitations in ADLs and mobility as middle-aged persons advance into later life. Middle-aged persons with depressive symptoms may be at greater risk for losing their functional independence as they age. J Am Geriatr Soc 58:551–556, 2010.

Key words: depression; functional status; outcomes; aging; disability

In aging populations, the ability to perform basic activities of daily living (ADLs) is a critical health outcome. Disability with basic tasks such as ADLs and walking short distances rises rapidly with age and becomes common in old age.1,2 These disabilities severely affect older people’s independence and quality of life. They impose considerable burden on family caregivers, are the principal indications for nursing home placement, and are associated with significantly shorter life expectancy.3–6

Multiple studies have demonstrated that older adults with depressive symptoms are more likely to be and become disabled.7–15 Similarly, studies in middle-aged populations show strong associations between depressive symptoms and health-related quality of life and work-related disability.16–18 However, most studies examining the relationship between depression and disability have been cross-sectional or of short duration, and it is not known whether middle-aged persons with depressive symptoms are at higher risk for later-life disability. This gap in understanding is an important deficiency in understanding the link between depressive symptoms and older age disability. This is particularly the case in light of recent conceptualizations of late-life disability and successful aging that recognize disablement as a life-course process that starts long before the disabilities of
old age are clinically apparent. This life-course approach to disability has particular relevance to depression. Unlike catastrophic causes of disability such as hip fracture and stroke, the effect of depressive symptoms is likely to be slow, yet progressive. Understanding whether middle-aged persons with depressive symptoms are at higher risk for disability as they enter later life has important implications for the management of depression and prevention of later-life disability.

To address this question, a study was conducted of subjects who were aged 50 to 61 when first enrolled in the Health and Retirement Study (HRS) in 1992. The study examined whether subjects with high levels of depressive symptoms were more likely to develop persistent difficulty in ADLs and mobility functioning over 12 years as these subjects entered old age. This long duration of follow-up provides a unique opportunity to examine the long-term effect of midlife depressive symptoms on the disabilities that threaten independence in old age.

METHODS

Subjects

Subjects enrolled in 1992 in the first wave of the HRS were used. The HRS is a nationally representative study of community-living adults born between 1931 and 1941 (aged 50–61 at enrollment). The HRS interviewed subjects every 2 years with the goal of examining changes in wealth and health as people transition from work to retirement and into old age.

Nine thousand seven hundred forty-eight subjects were enrolled in the 1992 wave of HRS. Because this study was examining the development of incident functional difficulties, subjects who already had reported difficulty with ADLs or walking (n = 1,845) were excluded; 68 subjects who had died by the next wave (1994) were also excluded, leaving 7,835 subjects eligible for the analytical cohort. Of these, 323 were excluded because they did not complete the depression survey in 1992, and 305 were excluded because they did not have follow-up data on functional outcomes, leaving a final sample size of 7,207 subjects.

Measures

Depressive Symptoms

Depressive symptoms were measured using the 11-item Center for Epidemiologic Studies Depression Scale (CES-D 11). The CES-D 11 asks subjects to rate the frequency of 11 symptoms of depression (over the previous week on a 4-point scale: rarely or none of the time, some of the time, most of the time, or all of the time). Each symptom is scored from 0 to 3, resulting in a total score of 0 to 33. The CES-D 11 is a shortened version of the CES-D 20, a commonly used index of depressive symptoms. The CES-D 11 retains the factor structure and almost all (87%) of the variance of the CES-D 20. Based on prior recommendations, subjects with CES-D 11 scores of 9 or more were classified as having significant depressive symptoms. This is approximately equivalent to a score of 16 on the CES-D 20. Because the CES-D 11 was administered only at the baseline interview in 1992, it was not possible to examine how depressive symptoms and disability changed together over time.

Mobility and ADL Difficulty

The outcome measure was persistent difficulty with basic mobility and ADL tasks over 12 years of follow-up. These two domains of functioning were chosen, because difficulty with these tasks is widely viewed as a threat to the independence of older persons. Subjects were classified as having a mobility difficulty if they reported difficulty walking several blocks or climbing one flight of stairs. Subjects were classified as having difficulty with ADLs if they reported difficulty with bathing, dressing, transferring from a bed to a chair, rising from a chair, using a toilet, or eating. The primary outcome was persistent difficulty with mobility or an ADL. Because these functional difficulties are often transient, subjects were classified as having a persistent difficulty only if they reported the difficulty on two consecutive waves. Subjects who had difficulty on one wave and died before the next wave were also classified as having a persistent difficulty.

To examine how often episodes of disability were transient and persistent, analyses were conducted in which subjects who reported disability (based on the primary outcome measure of ADL or mobility disability) on the first follow-up wave in 1994 were followed, and the persistence of disability over time was examined. Of those reporting disability in 1994, 60% were disabled in 1996 and were thus classified as persistently disabled in the analysis. Of those classified as persistently disabled in 1996, 14% subsequently recovered. This supports the approach of requiring disability on two consecutive waves to classify a subject as persistently disabled. Sixty-two percent of those who “recovered” by 1996 became disabled again or died during follow-up.

Other Measures

Demographic characteristics such as age, race, and education level were measured according to self-report. Other chronic medical conditions such as hypertension and diabetes mellitus were measured by asking the subject whether a doctor had ever told them they had the condition. Measures of socioeconomic status (SES) included years of education, income, and total net worth. Subjects were classified as engaging in frequent physical activity if they reported in engaging in at least light physical activity three or more times per week. Subjects were also asked whether they had difficulty with several higher-level measures of functioning, including the ability to jog 1 mile or climb several flights of stairs.

Analysis

The analyses used the sampling and design weights provided by the HRS to account for the probability of selection and clustering in HRS sample selection. Kaplan-Meier curves were constructed to compare the time to persistent difficulty with mobility or ADL function in subjects with and without depression at baseline. Although subjects were not classified as having persistent difficulty unless they reported difficulty on two consecutive waves, mobility or ADL difficulty was classified as having occurred in the wave in which it was first reported. Subjects who died without previously reporting difficulty were censored on the last wave in which they were interviewed.
Subjects who were lost to follow-up before the final interview (2004) were also censored as of the last wave in which they were interviewed. One thousand one hundred sixty (16.1%) subjects were censored before 2004.

Proportional hazards survival analysis was used to calculate the unadjusted and adjusted hazard ratio for the association between depression and subsequent mobility or ADL difficulty. To determine the independent association between depressive symptoms and mobility or ADL difficulty, age; sex; race; whether the subject was employed at least 20 hours a week; income; net worth; the presence of hypertension, diabetes mellitus, chronic lung disease, or arthritis; history of myocardial infarction, congestive heart failure, or stroke; body mass index (4 categories); current smoking; significant physical activity; difficulty jogging 1 mile; and difficulty climbing several flights of stairs were adjusted for. These analyses were repeated for each component (mobility and ADL difficulty) of the outcome.

To examine whether there was a dose-response relationship between depression and disability, two additional analyses were conducted. First, subjects were divided into approximate tertiles based upon their CES-D score, and the hypothesis was tested that there was a trend toward greater disability risk with worse depression score. Second, CES-D score was entered into the proportional hazards model as a continuous variable to test the hypothesis that higher CES-D scores were associated with greater disability risk across the full range of scores.

Finally, whether the association between depression and disability (mobility or ADL difficulty) differed between selected subgroups (age, sex, net worth, obesity, and exercise) was examined by calculating P-values for statistical interaction.

RESULTS
Characteristics of Subjects
Eight hundred eighty-seven (12%) subjects scored 9 or higher on the CES-D 11 and were classified as having significant depressive symptoms. Subjects with depressive symptoms were of similar age to subjects without depressive symptoms (56) but were more likely to be female (60% vs 51%, P<.001) and less likely to be white (71% vs 85%) (Table 1). They had lower SES according to all measures, including lower total net worth ($51,000 vs $134,000, P<.001). They had higher rates of many comorbid conditions, particularly hypertension (44% vs 33%, P<.001), and were more likely to be smokers (34% vs 24%, P<.001). They were also less likely to exercise three or more times a week (54% vs 61%, P=.001).

Relationship Between Depressive Symptoms and Functional Difficulties
Over 12 years of follow-up, subjects with depressive symptoms were more likely to reach the primary outcome measure of persistent disability with mobility or ADL function (Table 2, Figure 1) (45% vs 23%, hazard ratio (HR) = 2.33, 95% confidence interval (CI) = 2.06–2.63). As seen in the parallel Kaplan-Meier curves, the risk was relatively constant throughout the 12 years of follow-up. After adjusting for age, sex, measures of SES, comorbid conditions, body mass index, smoking, exercise, difficulty jogging 1 mile, and difficulty climbing several flights of stairs, the risk was attenuated but still statistically significant (HR = 1.44, 95% CI = 1.25–1.66). The group of variables that had the largest effect on explaining the association between depression and the development of functional difficulty were the SES variables (education, income, and net worth) which reduced the HR to 1.71 (95% CI = 1.50–1.96).

Of those reaching the primary endpoint of persistent mobility ADL difficulty, 62% had mobility difficulty with...
Table 2. Relationship Between Depression and the Development of Mobility and Activity of Daily Living (ADL) Difficulty

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Group</th>
<th>Outcome Rate, %</th>
<th>Unadjusted</th>
<th>Adjusted*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mobility/ADL</td>
<td>No depression</td>
<td>23</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>difficulty</td>
<td>Depression</td>
<td>45</td>
<td>2.33 (2.06–2.63)</td>
<td>1.44 (1.25–1.66)</td>
</tr>
<tr>
<td>Mobility</td>
<td>No depression</td>
<td>21</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>difficulty</td>
<td>Depression</td>
<td>41</td>
<td>2.32 (2.05–2.64)</td>
<td>1.40 (1.20–1.62)</td>
</tr>
<tr>
<td>ADL</td>
<td>No depression</td>
<td>8</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>difficulty</td>
<td>Depression</td>
<td>20</td>
<td>2.74 (2.33–3.23)</td>
<td>1.71 (1.44–2.04)</td>
</tr>
</tbody>
</table>

*Adjusted for age, sex, race, education, income, net worth, hypertension, diabetes mellitus, cancer, chronic lung disease, myocardial infarction, congestive heart failure, stroke, current smoker, body mass index, exercise, difficulty jogging 1 mile, and difficulty climbing several flights of stairs.

Tests for interaction suggested that the relationship between depression and disability may be greater in men (HR = 1.77, 95% CI = 1.47–2.14) than women (HR = 1.22, 95% CI = 0.99–1.51) (P for interaction .02) and in those aged 50 to 55 (HR = 1.62, 95% CI = 1.36–1.94) than those aged 56 to 61 (HR = 1.26, 95% CI = 1.01–1.57) (P for interaction <.01).

**DISCUSSION**

It was found that middle-aged subjects with depressive symptoms were more likely than those without to develop difficulty with mobility and ADLs over 12 years of follow-up. Difficulty in ADLs and mobility tasks are strongly associated with the need for personal assistance. Therefore, the results suggest that middle-aged persons with depressive symptoms will be at higher risk for becoming disabled and losing their independence as they age.

In unadjusted analyses, subjects with depressive symptoms had more than twice the risk of those without of becoming disabled. Subjects with depressive symptoms were different at baseline from those without in many risk factors that put them at higher risk for disability, including more comorbidity, lower SES, and worse health status. Although adjustment for these factors, especially SES, explained much of the risk associated with depressive symptoms, even after adjustment for all these factors, subjects with depressive symptoms were at 40% higher risk of developing difficulty in mobility or ADL function.

Although there is extensive literature linking depression to disability in older adults, most prior studies have been cross-sectional or had short follow-up. Furthermore, subjects in most studies were already of advanced age at the time of enrollment. The current study is one of the first to be informed by a conceptual framework that used a life-course approach. Distinctive features of the study were the enrollment of a predominantly middle-aged cohort free of significant disability at baseline that was then followed for an extended length of time as they advanced into later life. The life-course approach to the study of potential risk factors for disability is important, because most late-life disability is believed to be the result of an insidious process in which risk factors for disablement accumulate over many years and slowly exert deleterious effects that impair the ability to live independently. Although this study had longer follow-up than previous investigations, there is a need to further expand the life-course approach to depression and disability by including subjects at younger and older ages and following the progression of depression and disability over time.

The recognition of disability as a life-course process may have important implications for the prevention or delay of disability. For example, virtually all intervention efforts to prevent late-life disability have focused on older populations. In general, the magnitude of disability prevention has been modest. However, if disability develops insidiously over many years, it may be more effective to focus prevention efforts on earlier age groups. In some respects, the prevention of disability may be similar to the prevention of coronary artery disease, in which prevention interventions are initiated decades before coronary disease may become clinically apparent.

![Figure 1. Time to difficulty with activities of daily living or mobility (difficulty walking several blocks or up a flight of stairs) in subjects with and without depression.](image-url)
Although this study demonstrated an independent relationship between middle-life depression and later-life functional limitations, it is unknown whether treatment of depression in middle life will prevent disability in later life. The IMPACT intervention demonstrated that collaborative primary care–based management in late life effectively treats depression and improves physical function. It is not known whether more-effective management of midlife depression will also be effective at preventing later-life disability. The recognition that subjects with depressive symptoms are at high risk for late-life disability might also justify additional interventions such as physical activity interventions that lower disability risk regardless of its effect on depression.

There are several methodological considerations that should be addressed. First, it is not known who was treated for depression and therefore whether treatment modifies the risk for functional limitations. Second, it is not known whether depressive symptoms in the subjects were chronic or transient. Therefore, whether the duration of symptoms affects disability cannot be identified. Third, although the ability to adjust for confounders of the relationship between depression and disability exceeded that of most other studies, the adjustment may have been incomplete. For example, data were unavailable on the severity of individual comorbid conditions, and there were limited data on health habits. Fourth, cognitive impairment may be an important confounder of the relationship between depression and disability, but the analyses did not adjust for midlife indicators of cognitive impairment. Fifth, although it was required that subjects be disabled on two consecutive interviews to be considered persistently disabled, it is possible that some of these subjects were disability free between interviews. Also, a small number of subjects who were disabled on two consecutive waves subsequently recovered from disability.

Another limitation of this study was the use of just a baseline measure of depression rather than a longitudinal measure. Depression is often episodic, and it is likely that the persistence and chronicity of depression is an important mediator of the relationship between disability and depression. In addition, the relationship between depression and functional limitations is probably bidirectional, with multiple independent pathways and feedback loops. It was not possible to examine an alternative pathway examining whether disability leads to depression. Fully describing this relationship would require examining changes in depression and functional status over multiple waves of data.

In summary, depressive symptoms significantly increase the likelihood that middle-aged persons will develop difficulty with activities that are important to independent functioning as they age. It will require further study to determine whether interventions focused on depression or other risk factors for disability modify this risk.

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REFERENCES


