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Depressive symptoms in middle age and the development of later life functional limitations: The long term impact of depressive symptoms

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Abstract

Objective—To determine if middle aged persons with depressive symptoms are at higher risk for developing ADL and mobility limitations as they advance into older age.

Design—Prospective cohort study

Setting and Participants—7207 community living participants in the 1992 wave of the Health and Retirement Study (HRS), a nationally representative sample of people age 50–61.

Measurements—Depressive symptoms were measured with CES-D 11, with scores of 9 or more (out of 33) classified as significant depressive symptoms. Difficulty with 5 activities of daily living and basic mobility tasks (walking several blocks or up one flight of stairs) was measured every 2 years through 2006. Our primary outcome was persistent difficulty with either ADL or mobility, defined as difficulty on 2 consecutive waves.

Results—887 (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 our primary outcome measure of either persistent difficulty with mobility or difficulty with ADL function (45% vs 23%, Cox HR=2.33, 95% CI, 2.06–2.63). After adjusting for age, gender, measures of SES, comorbid conditions, high BMI, smoking, exercise, difficulty jogging one 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 basic activities and daily living and mobility as middle aged persons advance into later life. Middle age persons with depressive symptoms may be at greater risk for losing their functional independence as they age.

In aging populations, the ability to do basic tasks of daily life is a critical health outcome. Disability with basic tasks such as activities of daily living or walking a short distance rises rapidly with age and becomes common in old age[1,2]. These disabilities severely impact the independence and quality of life of older people. They impose considerable burden on family

caregivers, are the principal indications for nursing home placement, and are associated with significantly decreased life expectancy [3–6].

Multiple studies have demonstrated that elders 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 either 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 our understanding of 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 [19,20]. This life course approach to disability has particular relevance to depression. Unlike catastrophic causes of disability such as hip fracture and stroke, the impact of depressive symptoms is likely to be slow, yet progressive [21]. Understanding whether middle age 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, we conducted a study of subjects who were age 50–61 when first enrolled in the Health and Retirement Study (HRS) in 1992. We examined whether subjects with high levels of depressive symptoms were more likely to develop persistent difficulty in ADL 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 impact of midlife depressive symptoms on the disabilities that threaten independence in old age.

Methods

Subjects

We used subjects enrolled in 1992 in the first wave of the Health and Retirement Study (HRS) [22]. The HRS is a nationally representative study of community living adults born between 1931 and 1941 (age 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.

9748 subjects were enrolled in the 1992 wave of HRS. Since our interest was in the development of incident functional difficulties, we excluded subjects who already had reported difficulty with activities of daily living or walking ($n=1845$). We also excluded 68 subjects who died by the next wave (1994). Therefore 7835 subjects were eligible for our analytic 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 7207 subjects.

Measures

Depressive Symptoms—Depressive symptoms were measured using the 11-item Center for Epidemiologic Studies Depression Scale (CES-D-11) [23]. The CES-D-11 asks subjects to rate the frequency of 11 symptoms of depression (over the past 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 0–3, resulting in a total score of 0–33. 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, we classified subjects with CES-D 11 scores of 9 or more as having

significant depressive symptoms[24]. This is approximately equivalent to a score of 16 on the CES-D 20. Because the CES-D 11 was only administered at the baseline interview in 1992, we were not able to examine how depressive symptoms and disability changed together over time.

Mobility/ ADL difficulty—Our outcome measure was persistent difficulty with basic mobility and ADL tasks over 12 years of follow-up[25]. We chose these two domains of functioning because difficulty with these tasks is widely viewed as a threat to the independence of older persons[2]. 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 ADL if they reported difficulty with bathing, dressing, transferring from a bed to a chair, or out of a chair, using a toilet, or eating. Our primary outcome was persistent difficulty with either mobility or an ADL. Since these functional difficulties are often transient, we only classified subjects as having a persistent difficulty if they reported the difficulty on two consecutive waves. We also classified subjects who had difficulty on one wave and died before the next wave as having a persistent difficulty[26].

To examine how often episodes of disability were transient and persistent, we conducted analyses in which we followed subjects who reported disability (based on our primary outcome measure of either ADL or mobility disability) on the first follow-up wave in 1994, and examined the persistence of disability over time. Among those reporting disability in 1994, 60% were disabled in 1996, and were thus classified as persistently disabled in our analysis. Of those classified as persistently disabled in 1996, 14% subsequently recovered. This supports our approach of requiring disability on 2 consecutive waves in order to classify a subject as persistently disabled. 62% of those who “recovered” by 1996 either became disabled again, or died during follow-up.

Other measures—Demographic characteristics such as age, race, and education level were measured by self-report. Other chronic medical conditions such as hypertension and diabetes were measured by asking the subject whether a doctor had ever told them they had the condition [24]. Measures of socio-economic status included years of education, income, and total net worth. Subjects were classified as engaging in frequent physical activity if they reported in engaging in light physical activity or vigorous exercise 3 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 a mile or climb several flights of stairs.

Analysis—Our analyses used the sampling and design weights provided by the HRS to account for the probability of selection and clustering in HRS sample selection[27].

We constructed Kaplan-Meier curves to compare the time to persistent difficulty with mobility or ADL function in subjects with and without depression at baseline. While 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. 1160 (22%) subjects were censored before 2004.

We used proportional hazards survival analysis to calculate both 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, we adjusted for age, gender, race, whether or not the subject was employed at least 20 hours a week, income, net worth, the presence of hypertension, diabetes, chronic lung

disease, arthritis, history of MI, CHF, stroke, BMI (4 categories), current smoking, significant physical activity, difficulty jogging one mile, and difficulty climbing several flights of stairs. We repeated these analyses for each component (mobility difficulty and ADL difficulty) of our outcome.

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

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

Results

Characteristics of Subjects

887 (12%) of 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 years in both groups) 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 on 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 3 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 our primary outcome measure of either persistent difficulty with mobility or difficulty with ADL function (table 2, figure) (45% vs 23%, $HR=2.33$, 95% 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, gender, measures of SES, comorbid conditions, high BMI, smoking, exercise, difficulty jogging one 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 impact on explaining the association between depression and the development of functional difficulty were the SES variables (education, income, and net worth) which reduced the Hazard ratio to 1.71 (95% CI 1.50–1.96).

Among those reaching the primary endpoint of either persistent mobility difficulty or persistent ADL difficulty, 62% had mobility difficulty without ADL difficulty, 7% had ADL difficulty without mobility difficulty, and 31% had both mobility and ADL difficulty. Depressive symptoms were also associated with persistent ADL difficulty (20% vs 8%, adjusted HR 1.71, 95% CI 1.44–2.04) and persistent mobility difficulty (41% vs 21%, adjusted HR 1.40, 95% CI 1.2–1.62) when each of these components of our primary outcome were examined separately.

Additional analyses suggested there was a dose response relationship between depression score and disability. Compared to subjects in the tertile with the lowest CES-D score, those in the middle tertile (HR 1.19, 95% CI 1.01–1.42) and highest tertile (HR 1.57, 95% CI 1.37–1.79) had progressively higher adjusted risks of developing disability (p for trend $<.001$). When CES-D score was entered as a continuous variable, each additional point was associated with a higher risk of disability (HR 1.04, 95% CI 1.03–1.06).

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), and in those age 50–55 (HR 1.62, 95% CI 1.36–1.94) than those age 56–61 (HR 1.26, 95% CI 1.01–1.57) (p for interaction $<.05$).

Discussion

We found that middle aged subjects with depressive symptoms were more likely than those without depressive symptoms to develop difficulty with mobility and basic ADL over 12 years of follow-up. Difficulty in basic ADL and mobility tasks are strongly associated with the need for personal assistance[5]. Therefore, our results suggest that middle age 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 over twice the risk of nondepressed subjects of becoming disabled. Subjects with depressive symptoms were very different at baseline than subjects without depressive symptoms in many risk factors that put them at higher risk for disability, including more comorbidity, lower SES, and worse health status. While 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.

While there is an extensive literature linking depression to disability in the elderly, most prior studies are either cross-sectional or have relatively short follow-up[7–9,11–15,18,28]. Further, subjects in most studies were already of advanced age at the time of enrollment. Our study is one of the first to be informed by a conceptual framework that utilized a life course approach. Distinctive features of our 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[2]. While our study has longer follow-up than previous investigations, there is a need to further expand the lifecourse approach to depression and disability by including subjects at both younger and older ages, and following the progression of both 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 relatively modest[29]. However, if disability actually 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 where prevention interventions are initiated decades before coronary disease may become clinically apparent.

While we demonstrated an independent relationship between middle life depression and later life functional limitations, we do not know 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.[30] It is not known whether more effective management of mid-life 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 impact on depression.

There are several methodologic considerations that should be considered. First, we do not know who was treated for depression, and therefore do not know whether treatment modifies the risk for functional limitations. Second, we do not know whether depressive symptoms in our subjects were chronic or transient. Therefore, we can not identify whether the duration of symptoms affects disability. Third, while our ability to adjust for confounders of the relationship between depression and disability exceeded that of most other studies, our adjustment may have been incomplete. For example, we did not have data on the severity of individual comorbid conditions, and had limited data on health habits. Fourth, cognitive impairment may be an important confounder of the relationship between depression and disability but our analyses did not adjust for mid-life indicators of cognitive impairment. Fifth, while we required subjects to be disabled on two consecutive interviews to be considered persistently disabled, it is possible some of these subjects had disability free interviews between waves. 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[15]. In addition, the relationship between depression and functional limitations is probably bidirectional with multiple independent pathways and feedback loops. We were not able 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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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.

Table 1

Baseline characteristics of study sample by depression status.

Characteristic*		No Depression (N=6320)	Depression (N=887)	P-Value [†]
Demographics	Age (mean, SD)	56.0 (3.2)	55.8 (3.3)	0.21
	Age 50–55, %	48	52	0.07
	Age 56–61, %	52	48	
	Female, %	51	60	<0.001
	White, %	85	71	<0.001
	Black, %	8	15	
	Hispanic, %	5	10	
	Other, %	2	4	
SES Measures	<12 years education, %	19	34	<0.001
	Income (median, IQR), %	\$45K (25–69)	\$27K (14–48)	<0.001 [‡]
	Net worth (median, IQR) %, %	\$134K (56–284)	\$51K (8–142)	<0.001 [‡]
Comorbid conditions	Hypertension, %	33	44	<0.001
	Diabetes, %	6	7	0.34
	Cancer, %	5	6	0.22
	Chronic lung disease, %	5	9	<0.001
	MI, %	3	6	<0.001
	CHF, %	0.5	2	<0.001
	Stroke, %	1	2	0.19
	Current smoker, %	24	34	<0.001
BMI	<25, %	38	38	0.42
	25–29, %	41	42	
	30–34, %	15	15	
	≥35, %	6	4	
Exercise	3 or more times/week, %	61	54	0.001
Mobility Difficulties	Jog a mile, %	61	70	<0.001
	Climb several flights of stairs, %	12	27	<0.001

[†] P-value by chi-square test for categorical variables and t-test for continuous variables.

[‡] Based on log-transformed values for those with positive income/net worth.

Table 2

Relationship between depression and the development of mobility and ADL difficulty

Outcome	Group	Outcome rate, %	Unadjusted Cox HR (95% CI)	Adjusted* Cox HR (95% CI)
Either mobility or ADL difficulty	No Depression(N=6320)	23	1.00	1.00
	Depression (N=887)	45	2.33 (2.06–2.63)	1.44 (1.25–1.66)
Mobility difficulty	No Depression (N=6319)	21	1.00	1.00
	Depression (N=886)	41	2.32 (2.05–2.64)	1.40 (1.20–1.62)
ADL difficulty	No Depression(N=6317)	8	1.00	1.00
	Depression (N=886)	20	2.74 (2.33–3.23)	1.71 (1.44–2.04)

* Adjusted for age, gender, race, education<12 years, income, net worth, hypertension, diabetes, cancer, chronic lung disease, mi, chf, stroke, current smoker, BMI category, exercise 3+ times/week, difficulty jogging 1 mile, difficulty climbing several flights of stairs.