

Higher Burden of Depression Among Older Women

The Effect of Onset, Persistence, and Mortality Over Time

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Context: The prevalence of depression is disproportionately higher in older women than men, yet the reasons for this sex difference are not clear.

Objective: To determine whether the higher burden of depression among older women than men might be attributable to sex differences in the onset (ie, first or recurrent episodes) or persistence of depression and/or to differential mortality among those who are depressed.

Design: Prospective cohort study.

Setting: General community in greater New Haven, Connecticut, from March 23, 1998, to August 31, 2005.

Participants: A total of 754 persons, 70 years or older, who were evaluated at 18-month intervals for 72 months.

Main Outcome Measures: The 3 outcome states were depressed, nondepressed, and death, with scores of 20 or more and less than 20 on the Center for Epidemiological Studies Depression Scale denoting depressed and nondepressed, respectively. The association between sex and the likelihood of 6 possible transitions (namely, from

nondepressed or depressed to nondepressed, depressed, or death) was evaluated over time.

Results: The prevalence of depression was substantially higher among women than men at each of the 5 time points ($P < .001$). In most cases, transitions between the nondepressed and depressed states were characterized by moderate to large absolute changes in depression scores (ie, ≥ 10 points). Adjusting for other demographic characteristics, women had a higher likelihood of transitioning from nondepressed to depressed (odds ratio, 2.02; 95% confidence interval, 1.39-2.94) and a lower likelihood of transitioning from depressed to nondepressed (odds ratio, 0.27; 95% confidence interval, 0.13-0.56) or death (odds ratio, 0.24; 95% confidence interval, 0.09-0.60).

Conclusion: Among older persons, the higher burden of depression in women than men seems to be attributable to a greater susceptibility to depression and, once depressed, to more persistent depression and a lower probability of death.

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WHEREAS MAJOR depression affects only about 1% to 2% of community-dwelling older persons,^{1,2} clinically significant depressive symptoms are more common. Often referred to as “depressed mood” or simply “depression,” clinically significant depressive symptoms affect between 8% and 20% of this population³⁻¹⁰ and are highly morbid.¹¹⁻²³ The burden of depression, however, is disproportionately higher among older women than men.^{2,24-31} Despite an expanding knowledge base about late-life depression,^{7,32} the reasons for this sex difference have remained poorly defined.

Efforts to explain the sex difference in the prevalence of depression have focused largely on evaluating associations be-

tween sex and exposure to risk factors for depression,²⁸ comparing sex differences in the perception of symptoms,^{33,34} and identifying environmental and personality factors that mediate the relationship between sex and depression.³⁵ An alternative approach, which has not yet been formally evaluated, is to determine whether sex differences in depression onset, persistence, and mortality might collectively account for the higher burden of depression among older women. While prior studies have evaluated sex differences in depression onset and persistence^{9,36-40} or in mortality among those who are depressed,^{18,41,42} they have been limited by the availability of data at only 2 time points, often at widely spaced intervals,^{9,18,36-38,40,42} or by a short follow-up.³⁶ To our knowledge, only 1 study³⁹ has considered the po-

tentially fluctuating course of depression over time, but this study had a short follow-up and included only depressed persons in its sample.

The objective of this prospective study was to determine whether the higher burden of depression among older women than men is attributable to sex differences in the onset of depression (ie, first or recurrent episodes) or persistence of depression over time and/or to differential mortality among those who are depressed. To achieve our objective, we evaluated possible transitions between 3 states—not depressed, depressed, and death—at 18-month intervals for 6 years among a large cohort of older men and women.

METHODS

STUDY POPULATION

Participants were members of the Precipitating Events Project, a longitudinal study of 754 community-dwelling persons 70 years or older.⁴³ The assembly of the cohort has been described in detail elsewhere.⁴³ In brief, potential participants were identified from 3157 age-eligible members of a health plan in New Haven. The primary inclusion criteria were English speaking and requiring no personal assistance with 4 key activities of daily living (ie, bathing, dressing, transferring from a chair, and walking). The participation rate was 75.2%.⁴³ During the 6-year follow-up between March 23, 1998, and August 31, 2005, 232 participants died after a median of 48 months, 27 dropped out of the study after a median of 24 months, and 18 were subsequently excluded because of participation by proxy after a median of 32 months. The Human Investigation Committee at Yale University approved the study.

DATA COLLECTION

The present study included data collected during in-home assessments that were completed at baseline and every 18 months for up to 72 months by trained research nurses who used standard procedures that have been described in detail elsewhere.⁴⁴ Demographic data included age, sex, race, and educational level. Medical comorbidity was ascertained based on the presence of 9 self-reported physician-diagnosed chronic conditions, including hypertension, myocardial infarction, congestive heart failure, stroke, diabetes mellitus, hip fracture, arthritis, chronic lung disease, and cancer (other than minor skin cancer). Cognitive status was assessed with the Mini-Mental State Examination of Folstein et al.⁴⁵ Deaths were ascertained by review of local obituaries and/or from an informant.

ASSESSMENT OF DEPRESSION

The 11-item Center for Epidemiological Studies Depression Scale (CES-D)⁴⁶ was used to assess depressive symptoms in the previous week during each of the 5 time points (ie, baseline and 18, 36, 54, and 72 months). Prior studies^{47,48} of older persons report test-retest reliability statistics of 0.82 or higher on the shortened form of the CES-D. As in several prior studies,^{17,18,49} scores were transformed using the procedure recommended by Kohout et al⁵⁰ to make it compatible with the full 20-item instrument. Total scores range from 0 to 60, with higher scores indicating more depressive symptoms. While a CES-D score of 16 is most commonly used to distinguish between depressed and nondepressed persons in mixed-age samples, a cut point of 20 offers a more stringent approach to the classification of

depressed mood among older persons.^{14,17,51-53} A CES-D score of 20 or higher has been shown to predict outcomes related to well-being and functioning and diagnostic measures of depression,³⁹ and it has been used in several prior epidemiological studies^{11,17,53} of depression in elderly persons. Data on depression were complete for 100% of the participants at baseline and 95.2%, 92.8%, 90.7%, and 89.8% of the nondecedents at 18, 36, 54, and 72 months, respectively.

STATISTICAL ANALYSIS

We determined the association, at baseline, between depression and the characteristics of the participants using χ^2 or *t* test statistics. We then compared the prevalence of depression between men and women at each time point using the χ^2 statistic. For each of the 18-month intervals, we calculated rates by sex for 6 possible transitions, defined based on the 3 outcome states: nondepressed, depressed, and death. χ^2 or Fisher exact statistics were used to evaluate the bivariate associations between sex and the 6 possible transitions for each time interval. Because the number of participants was relatively small for some of the transitions, the power to detect statistically significant differences in the transition rates according to sex may not have been adequate for all comparisons. Furthermore, to account for the many comparisons, *P* values were determined according to the Hochberg method.⁵⁴

To determine whether the observed transitions were clinically meaningful, we calculated the percentage of transitions that represented absolute changes in the CES-D scores of 1 to 3 (small), 4 to 9 (moderate), 10 to 19 (large), and 20 or more (very large) points for each time interval, and we subsequently determined whether the distribution of these percentages differed by sex using the χ^2 statistic.

Last, we evaluated the association between sex and the likelihood of the 6 possible transitions over time using longitudinal methods that optimized statistical power and accounted for potential correlation among depression scores. Specifically, we ran generalized multinomial logit models for nominal outcomes that were estimated with a generalized estimating equation and used exchangeable correlation structures.⁵⁵ The first longitudinal model included participants who were nondepressed at the beginning of any 18-month interval, with participants who were nondepressed during the entire interval (ie, at 2 consecutive 18-month time points) serving as the comparison group. The second longitudinal model included participants who were depressed at the beginning of any 18-month interval, with participants who were depressed during the entire interval serving as the comparison group. The magnitude of association was denoted by odds ratios, which were subsequently adjusted for age, race (white vs other), educational level, number of chronic conditions, and Mini-Mental State Examination score.

All statistical tests were 2-tailed, and *P* < .05 was considered statistically significant. The longitudinal models were performed using SUDAAN survey data analysis software, version 9.0⁵⁶; all other analyses were performed using SAS statistical software, version 9.1.⁵⁷

RESULTS

Table 1 provides the characteristics of the study participants over 6 years. At baseline, participants were a mean age of 78.4 years; about two-thirds were women, and most were white. On average, participants had a high school education, had 2 chronic conditions, and were cognitively intact. Compared with the nondepressed participants, par-

Table 1. Characteristics of Study Participants Over 6 Years^a

Characteristic	Baseline (N=754)	18 mo (n=675)	36 mo (n=612)	54 mo (n=538)	72 mo (n=471)
Age, y	78.4 (5.3)	79.6 (5.1)	80.9 (5.1)	82.2 (4.9)	83.7 (4.8)
Female sex ^b	487 (64.6)	439 (65.0)	405 (66.2)	359 (66.7)	310 (65.8)
Non-Hispanic white race ^b	682 (90.5)	609 (90.2)	550 (89.9)	483 (89.8)	423 (89.8)
Education, y	12.0 (2.9)	12.0 (2.8)	12.0 (2.8)	12.0 (2.8)	12.1 (2.8)
No. of chronic conditions ^c	1.9 (1.3)	2.1 (1.3)	2.2 (1.3)	2.2 (1.3)	2.4 (1.3)
Cognitive status score ^d	26.8 (2.5)	26.4 (2.9)	26.3 (3.4)	25.5 (4.0)	25.3 (4.6)
Depression ^{b,e}					
Men	14 (5.2)	17 (7.2)	22 (10.6)	13 (7.3)	17 (10.6)
Women	86 (17.7)	99 (22.6)	102 (25.2)	96 (26.7)	74 (23.9)

^aData are given as mean (SD) unless otherwise indicated. The cumulative number of decedents was 46 at 18 months, 98 at 36 months, 166 at 54 months, and 232 at 72 months.

^bData are given as number (percentage) of participants at each time point.

^cThe 9 self-reported physician-diagnosed chronic conditions included hypertension, myocardial infarction, congestive heart failure, stroke, diabetes mellitus, hip fracture, arthritis, chronic lung disease, and cancer (other than minor skin cancer).

^dAs assessed by the Mini-Mental State Examination.

^ePercentages are based on the totals for men and women separately. At each time point, the rate was substantially higher among women than men ($P < .001$).

Table 2. Transition Rates Between the 3 Outcome States Over Time According to Sex^a

Transition	0-18 mo		18-36 mo		36-54 mo		54-72 mo	
	Men (n=244)	Women (n=386)	Men (n=212)	Women (n=329)	Men (n=183)	Women (n=289)	Men (n=164)	Women (n=257)
Nondepressed								
To nondepressed								
No. (%)	213 (87.3)	315 (81.6)	175 (82.5)	267 (81.2)	150 (82.0)	227 (78.5)	137 (83.5)	205 (79.8)
P value	.47		.74		.74		.74	
To depressed								
No. (%)	12 (4.9)	52 (13.5)	19 (9.0)	48 (14.6)	11 (6.0)	40 (13.8)	12 (7.3)	26 (10.1)
P value	.006		.47		.08		.74	
To death								
No. (%)	19 (7.8)	19 (4.9)	18 (8.5)	14 (4.3)	22 (12.0)	22 (7.6)	15 (9.1)	26 (10.1)
P value	.74		.42		.74		.74	
	(n=14)	(n=77)	(n=16)	(n=93)	(n=20)	(n=99)	(n=13)	(n=91)
Depressed								
To nondepressed								
No. (%)	6 (42.9)	25 (32.5)	8 (50.0)	33 (35.5)	15 (75.0)	33 (33.3)	7 (53.8)	30 (33.0)
P value	.99		.99		.006		.99	
To depressed								
No. (%)	5 (35.7)	47 (61.0)	3 (18.8)	51 (54.8)	2 (10.0)	53 (53.5)	5 (38.5)	47 (51.6)
P value	.63		.08		.004		.99	
To death								
No. (%)	3 (21.4)	5 (6.5)	5 (31.2)	9 (9.7)	3 (15.0)	13 (13.1)	1 (7.7)	13 (14.3)
P value	.72		.28		.99		.99	

^aTransition rates were calculated for participants who had data on depression or death at each of the 2 time points defining the relevant follow-up interval. Column percentages for each baseline state (nondepressed and depressed) at each time point may not total 100 because of rounding. P values were determined according to the Hochberg method for multiple comparisons.⁵⁴

Participants who were depressed at baseline were less educated ($P < .001$), had more chronic conditions ($P = .003$), had lower Mini-Mental State Examination scores ($P = .002$), and were more likely to be women ($P < .0001$). The proportion of women did not change appreciably over time, while the burden of chronic conditions increased modestly. At baseline and each subsequent time point, the prevalence of depression was substantially higher among women than men ($P < .001$), with the greatest absolute difference observed at 54 months. Furthermore, of the 269 participants (35.7%) who were depressed at some point during

the 72 months of follow-up, 48 (17.8%), 30 (11.2%), 17 (6.3%), and 12 (4.5%) were depressed during 2, 3, 4, and 5 consecutive time points, respectively, with more women experiencing depression at subsequent time points compared with men ($P < .01$).

Table 2 provides the transition rates between the 3 outcome states over the 18-month intervals according to sex. With only a few exceptions, the rates were comparable across the 4 intervals. Among participants who were nondepressed, women generally had higher rates of transitioning to depressed and lower rates of remaining non-

depressed or transitioning to death. Among those who were depressed, women had higher rates of remaining depressed and lower rates of transitioning to nondepressed or death, with 1 exception. Women had a higher rate of transitioning from depressed to death during the 54- to 72-month interval, although this difference was not statistically significant.

As shown in the **Figure**, A, most transitions from nondepressed to depressed were based on moderate to large absolute changes in CES-D scores (ie, ≥ 10 points); small changes in the range of 1 to 3 points were observed for no more than 15% of the transitions during any of the 18-month intervals. Similar results were found for transitions from depressed to nondepressed (Figure, B). There were no differences in the distribution of change scores by sex for either set of transitions (results not shown).

Table 3 presents the unadjusted and adjusted odds ratios derived from the longitudinal models evaluating the association between sex and the likelihood of the 6 transitions between the 3 outcome states over 6 years. Among those who were nondepressed, women were more likely to transition to a depressed state, with an adjusted odds ratio of 2.02. Among those who were depressed, women were less likely to transition to nondepressed and to death, with adjusted odds ratios of 0.27 and 0.24, respectively. There was no significant association between sex and transitioning from nondepressed to death.

COMMENT

In this longitudinal study, which included multiple assessments over 6 years, we confirmed that the prevalence of depression is substantially higher among older women than men. More important, we found that this sex difference is attributable to a greater susceptibility to depression and, once depressed, to more persistent depression and a lower probability of death in older women.

Late-life depression is a significant clinical and public health problem because it is common^{6-9,37} and costly^{58,59} and is associated with disability^{8,15,17,19} and other adverse outcomes, including rehospitalization and death among those with chronic obstructive pulmonary disease,⁶⁰ myocardial infarction,⁶¹⁻⁶³ and stroke.⁶⁴ Despite these negative consequences, there is considerable uncertainty about why the prevalence of late-life depression is disproportionately higher in women than men. To our knowledge, the present study is the first to evaluate whether sex differences in depression onset, persistence, and mortality might collectively account for the higher burden of depression among older women.

With 1 exception,⁹ prior studies of community-living older persons have found no evidence of a sex difference in either the onset^{9,36,37,40} or persistence^{9,36,38,39} of depression. These studies,^{9,37,39,40} however, have generally included only 1 follow-up assessment of depression at an interval no shorter than 2 years. The inability to account for fluctuations in depression over time (ie, recurrent depression) may have a substantial effect on estimates of depression onset. In contrast, we evaluated transitions into and out of depression states at 18-month intervals for 6 years and used longitudinal methods that

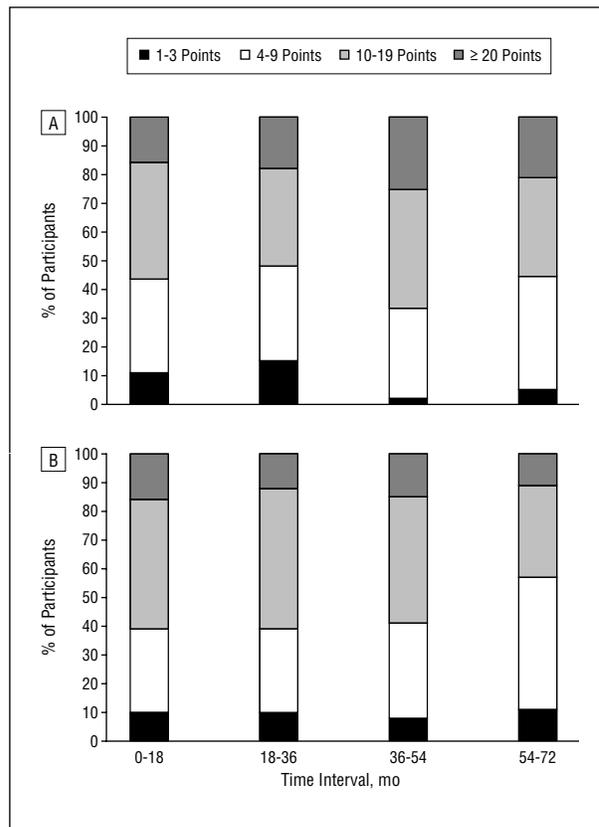


Figure. Change in Center for Epidemiological Studies Depression Scale score (by points) among participants who transitioned from nondepressed to depressed (A) and from depressed to nondepressed (B). In A, there were 64 participants from 0 to 18 months, 67 participants from 18 to 36 months, 51 participants from 36 to 54 months, and 38 participants from 54 to 72 months. In B, there were 31 participants from 0 to 18 months, 41 participants from 18 to 36 months, 48 participants from 36 to 54 months, and 37 participants from 54 to 72 months. Time 0 indicates baseline.

addressed potential problems related to low power for any single time interval. Low self-esteem, helplessness, and low social status have been shown to differentially increase the risk of depression onset in women younger than 65 years compared with men of the same age.⁶⁵ Additional research is needed to determine the cause of sex differences in depression onset among older persons.

The consistency of our findings over 4 different time intervals provides strong evidence that depression is more likely to persist in older women than men. This sex difference in the persistence of depression is somewhat surprising because women are more likely than men to receive pharmacologic and nonpharmacologic treatment for depression.⁶⁶⁻⁷⁰ Whether women are treated less aggressively than men for late-life depression or are less likely to respond to conventional treatment is not known⁷¹⁻⁷³ but should be the focus of future research. In addition, nearly 40% of the depressed participants in this study were depressed during at least 2 consecutive time points, highlighting the need to initiate and potentially maintain antidepressant treatment after resolution of the initial depressive episode.⁷⁴

As in prior studies,^{18,41,42} we found that older women are less likely than men to die when depressed, providing a third explanation for the sex difference in the preva-

Table 3. Longitudinal Assessment of Transitions Over the 6 Years Among Women Relative to Men

Transition	Unadjusted Data		Adjusted Data	
	Odds Ratio (95% Confidence Interval)	P Value	Odds Ratio (95% Confidence Interval) ^a	P Value
Nondepressed				
To nondepressed	1 [Reference]	NA	1 [Reference]	NA
To depressed	2.06 (1.45-2.92)	<.001	2.02 (1.39-2.94)	<.001
To death	0.74 (0.54-1.02)	.07	0.79 (0.56-1.12)	.19
Depressed				
To depressed	1 [Reference]	NA	1 [Reference]	NA
To nondepressed	0.28 (0.15-0.51)	<.001	0.27 (0.13-0.56)	<.001
To death	0.25 (0.11-0.55)	<.001	0.24 (0.09-0.60)	.003

Abbreviation: NA, data not applicable.

^aAdjusted for age (in years), race (white vs other), education (in years), number of chronic conditions, and Mini-Mental State Examination score.

lence of depression. Of course, older men generally have higher mortality rates than older women, irrespective of depression,⁷⁵ as was observed in the present study. Nevertheless, the mortality difference we observed by sex was marked, with a nearly 3-fold difference in the odds ratios for participants who were depressed compared with those who were not depressed.

The availability of 5 waves of data over a 6-year period provides the best information, to date, on how depression onset, persistence, and mortality collectively influence the prevalence of depression. Because these factors are highly interrelated, we were unable to determine their relative contribution to the prevalence of depression. Prevalence, for example, is a function of incidence and duration, while duration is a function of persistence and mortality.

Because information regarding participants' depression status before the baseline interview was not available, we cannot determine if participants' first transition from a nondepressed to a depressed state represents incident depression. Given the preponderance of depression among women compared with men in nonelderly samples,⁷⁶⁻⁷⁸ it is possible that our findings represent the continuation of a sex-related pattern of depression established earlier in life. Future studies should evaluate whether sex differences in the onset and persistence of depression during youth and middle age may help to explain reasons for sex differences in depression patterns in older age.

In the absence of a diagnostic measure, such as the Structured Clinical Interview for *DSM-IV*,⁷⁹ we were unable to determine the prevalence of major depression among the study participants. However, we used a cut point of 20 or greater on the CES-D to identify depressed participants at each time point. This cut point has previously been shown to enhance the likelihood of detecting depressed mood among community-living older persons.^{14,17,51-53,80} Furthermore, the moderate to large changes in the CES-D scores over time, regardless of sex, indicate clinically meaningful transitions between depression states. The baseline rate of depression in our study is somewhat higher than rates reported in other studies^{17,80} of older persons that have used the more stringent cut point of 20 or greater on the CES-D. This difference may be explained by the higher mean age and

more diverse racial composition of our sample compared with the samples in these other studies.

Because our study participants were members of a single health plan, nondisabled, and at least aged 70 years at baseline, the generalizability of our findings to other older adult populations may be questioned. As previously noted, however,⁴³ the demographic characteristics of our study population, including years of education, closely mirror those of persons 70 years or older in New Haven County, Connecticut, which, in turn, are comparable to those in the United States as a whole, with the exception of race. New Haven County has more non-Hispanic whites in this age group than in the United States (91% vs 84%).⁸¹ Given that African Americans have a higher prevalence of persistent depression compared with non-Hispanic whites,⁸² future research should explore whether the relationship between sex and transitions across depression states is modified by race using data that more closely reflect the racial composition of older adults in the United States. Furthermore, generalizability depends not only on the characteristics of the study population but also on its stability over time.⁸³ The high participation rate, completeness of data collection, and low rate of attrition for reasons other than death all enhance the generalizability of our findings⁸² and at least partially offset the absence of a population-based sample.

In summary, the higher burden of depression in older women than men seems to be attributable to a greater susceptibility to depression and, once depressed, to more persistent depression and a lower probability of death. Additional research is needed to determine the cause of these sex differences so that more effective strategies can be developed to detect and manage depression in this population.

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