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Association of social support with mild cognitive impairment and dementia among older women: the Women's Health Initiative Memory Study

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Abstract

Background: Social support may be a modifiable risk factor for cognitive impairment. However, few long-term, large prospective studies have examined associations of various forms of social support with incident mild cognitive impairment (MCI) and dementia.

Objective: To examine associations of perceived social support with incident MCI and dementia among community-dwelling older women.

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CONFLICT OF INTEREST/DISCLOSURE STATEMENT

The authors have no conflict of interest to report.

Methods: This prospective cohort study included 6,670 women from the Women's Health Initiative Memory Study who were cognitively unimpaired at enrollment. We used Cox proportional hazards models to assess associations between perceived social support with incident MCI, dementia, or either MCI/dementia during an average 10.7 (SD=6.1)-year follow-up. Modelling was repeated for emotional/information support, affection support, tangible support, and positive social interaction subscales of social support.

Results: Among 6,670 women (average age=70 years[SD=3.8]; 97.0% non-Hispanic/Latina; 89.8% White), greater perceived social support was associated with lower risk of MCI/dementia after adjustment for age, ethnicity, race, hormone therapy, education, income, diabetes, hypertension, and body mass index (Tertile [T]3 vs. T1: HR=0.85, 95%CI 0.74–0.99; p_{trend}=0.08). Associations were significant for emotional/information support (T3 vs. T1: HR=0.84, 95%CI 0.72–0.97; p_{trend}=0.04) and positive social interaction (T3 vs. T1: HR=0.85, 95%CI 0.73–0.99; p_{trend}=0.06) subscales. Associations were attenuated and not significant after adjustment for depressive symptom severity.

Conclusion: Perceived social support, emotional/information support, and positive social interaction were associated with incident MCI/dementia among older women. Results were not significant after adjustment for depressive symptom severity. Improving social support may reduce risk of MCI and dementia in older women.

INTRODUCTION

Approximately 6.2 million adults aged 65 or older are living with Alzheimer's Disease and related dementias in the United States, with women accounting for two-thirds of this estimate [1]. Women may be at increased risk of dementia due to biological (e.g., hormonal changes over time) and social (e.g., education) factors [2]. Identifying modifiable risk factors is important for developing strategies to reduce risk of age-related cognitive impairment. One potential modifiable risk factor for dementia may be low social support. Social support may provide resilience to stress [3], potentially lowering the risk of Alzheimer's disease and other dementias [4].

Social support can be defined as the perceived availability of social resources and support provided by others [5]. Social support includes emotional, instrumental, informational, and appraisal types of support [5–8]. Few large, long-term prospective studies have examined associations of social support with cognitive function [9–11] or dementia [12–14]. The association of social support with cognitive function may also differ by sex [9,10]. However, some longitudinal studies that examined dementia used social support questionnaires that were brief [12,13] or did not demonstrate strong psychometric properties [14].

The overall objective of this prospective cohort study was to examine associations of overall perceived social support with incident mild cognitive impairment (MCI) and dementia in a population of community-dwelling older women. We hypothesized that greater perceived

social support would be associated with lower risk of incident MCI/dementia. We also examined 4 subscales of social support to examine the association of specific types of social support with MCI/dementia.

METHODS

Study Population

This prospective study used data from the Women's Health Initiative Memory Study (WHIMS), an ancillary study to the Women's Health Initiative (WHI) Hormone Therapy (HT) trials. WHIMS investigated the effects of HT (estrogen alone or estrogen and progestin relative to placebo) on cognitive outcomes among 7,479 women who were 65–80 years old and free of cognitive impairment at randomization (1995–1998), with annual follow-up of cognitive outcomes through 2007 [15]. In 2008, WHIMS began annual telephone-administered cognitive assessments in the WHIMS-Epidemiology of Cognitive Health Outcomes (WHIMS-ECHO) study [16].

For the present study, women were followed for cognitive outcomes from WHIMS baseline in 1995–1998 until December 31, 2019. We first excluded 248 women with incomplete social support data. Then we excluded 230 women who were lost to follow-up after baseline. We also excluded 219 women with a history of coronary heart disease, 98 women with history of stroke, and 14 women with both histories [17,18]. This yielded a final analytic sample of 6,670 women. All study protocols were approved by the Fred Hutchinson Cancer Research Center Institutional Review Board. Women provided informed consent in writing or by telephone.

Measures

Social support.—Social support was assessed using 9 items from the 19-item Medical Outcomes Study Social Support Survey (MOS-SSS) at baseline [19]. Participants were presented the following prompt: "People sometimes look to others for help, friendship, or other types of support. Next are some questions about the support that you have. How often is each of the following kinds of support available to you if you need it?" Participants then rated 9 items to assess the amount of social support available to them (see Table 1 for full list of items). Responses to each item were rated on a five-point Likert scale: 1) None of the time; 2) A little of the time; 3) Some of the time; 4) Most of the time; and 5) All of the time. Ratings for all items were summed to generate a summary score ranging from 9 to 45, with higher scores indicating greater perceived social support.

There were four MOS-SSS subscales of interest: 1) emotional/information support (range = 4–20), 2) affection support (range = 1–5), 3) tangible support (range = 2–10), and 4) positive social interaction (range = 2–10). To assess dose-response associations, we created tertiles of MOS-SSS and its subscales, because clinically meaningful MOS-SSS categories have yet to be established. Tertile distributions are shown in Supplementary Table 1. The MOS-SSS had high internal consistency in the present study (Cronbach's α = 0.92).

Outcomes.—Our main outcome was time to either first incident MCI or first incident probable dementia (i.e., MCI/dementia), which was ascertained and adjudicated annually

until December 31, 2019. Secondarily, we examined associations with first incident MCI and first incident probable dementia separately. Full details of WHIMS outcomes ascertainment and adjudication are provided elsewhere [15]. Briefly, women completed the Modified Mini-Mental State Examination annually. Women scoring below specific cut points (<80 for those with 8 years of education and <88 for those with 9 years of education) completed a modified Consortium to Establish a Registry for Alzheimer's Disease, which is a battery of standardized neuropsychological tests. A physician with expertise in dementia diagnosis conducted a neuropsychiatric evaluation with optional blood assays and computerized tomography brain scan (without contrast) and then classified women as having no cognitive impairment, MCI based on Petersen's criteria [20], or probable dementia based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria [21]. The WHIMS Clinical Coordinating Center provided central adjudication of final classification by a panel consisting of a neurologist, geriatric psychiatrist, and geropsychologist. WHIMS-ECHO used a validated protocol of telephone-based cognitive assessments and informant interviews [22], and similar protocols to WHIMS for central adjudication of final classification of cognitive status.

Covariates.—Information on baseline covariates was derived from self-report or clinical measures. Covariates included age, ethnicity, race, hormone therapy (HT) trial arm, history of HT use, education level, history of diabetes, history of hypertension, body mass index (BMI; kg/m^2), smoking status, alcohol use, and depressive symptom severity. Depressive symptom severity was measured using the Burnam algorithm, which includes 6 items from the Center for Epidemiological Studies Depression Scale (CES-D) and 2 items from the Diagnostic Interview Schedule [23]. Burnam scores range from 0 to 1, where scores >0.06 suggest significant depressive symptom severity [23]. Self-identified ethnicity was categorized into two levels (Not Hispanic/Latina; Hispanic/Latina/Unknown/Not reported). For the analyses, self-identified race was categorized into three levels: 1) White; 2) Black; and 3) American Indian/Alaska Native, Asian, Native Hawaiian/Other Pacific Islander, more than one race, unknown, or not reported. Race and ethnicity were included in analyses to control for potential biases related to cognitive testing, as was performed in prior studies among the WHIMS cohort [24]. We did not include marital status as a covariate in our primary analyses, given the potential overlap with social support. However, we included marital status as a covariate in sensitivity analyses.

Statistical Analysis

Descriptive statistics.—Baseline characteristics were summarized across tertiles of perceived social support. Continuous variables were summarized using means and standard deviations or medians and interquartile ranges, if not normally distributed. Categorical variables were described using counts and percentages. Comparisons across tertiles of perceived social support were performed using analysis of variance or Kruskal-Wallis tests for continuous variables and Pearson's chi-squared test for categorical variables.

Cox proportional hazards regression.—Associations of perceived social support with cognitive outcomes were estimated using Cox proportional hazards regression models. Time was defined as the number of days from enrollment to date of the cognitive assessment

that triggered the first diagnosis of MCI or dementia, loss to follow-up, or December 31, 2019, whichever came first. Women who did not develop MCI or dementia were censored on the date of their last cognitive assessment. We used four sequentially adjusted models for each outcome. Model 1 was adjusted for age, ethnicity, race, HT trial arm, and history of HT use. Model 2 additionally adjusted for education, income, history of diabetes, history of hypertension, and BMI. Model 3 additionally adjusted for smoking and alcohol use. Model 4 additionally adjusted for depressive symptom severity as a continuous variable. *P* values for trend (p_{trend}) were calculated using social support as a continuous variable in the models. We repeated these procedures using the four MOS-SSS subscales. To account for missing covariate data, we employed multiple imputation analysis by chained equations using the *mice* package [25]. There were 10 imputed datasets and results were pooled for reported estimates. The proportional hazards assumption was tested using Schoenfeld residuals in complete case Model 4 for each outcome; non-proportional hazards were observed. Therefore, within proportional hazards models, we stratified by race, diabetes, and smoking for MCI models; age and smoking for dementia models; and age, race, and smoking for MCI/dementia models to account for potential time-dependence.

Sensitivity analyses.—We performed several sensitivity analyses. First, primary analyses were repeated using a complete case analysis approach. Second, to account for reverse causation, we repeated primary analyses after excluding women who were lost to follow-up or developed MCI/dementia during the first two years and first five years of follow-up. Third, we addressed selection bias, which may occur with participant censoring after enrollment [26]. To account for bias due to censoring before the last cognitive assessment in 2019, we applied stabilized inverse probability of censoring weights (IPCW), truncated at the 5th and 95th percentiles, to our primary analyses (see Supplementary Methods 1). Fourth, in post-hoc analyses, we stratified our main analysis by Burnam scores where scores ≤0.06 suggest no/minimal depressive symptom severity and scores >0.06 suggest significant depressive symptom severity [23]. Fifth, we repeated our primary analyses with marital status as a covariate. Sixth, we stratified our findings by Black and White race to evaluate racial differences in the association of social support with MCI/dementia.

All statistical analyses were conducted in R version 4.0.3. Statistical tests were two-tailed and P-values were considered statistically significant at $p < 0.05$.

RESULTS

Of the 6,670 women in our sample (mean age = 70.0 years; SD 3.8), 753 had incident MCI, 697 had probable dementia, and 1,197 had a first diagnosis of either incident MCI or probable dementia, during an average of 10.7 (SD 6.1) years of follow-up. Relative to women in the lowest tertile of social support, women in the highest tertile of social support had a higher proportion of >$35,000 income (52.4% vs. 35.1%), married or in a relationship (71.1% vs. 36.6%), baseline HT use (7.4% vs. 5.7%), never smoking (56.4% vs. 51.5%), and drinking alcohol in the past month (68.6% vs. 67.0%; Table 2). Women in the highest tertile of social support had lower depressive symptom severity than those in the lowest tertile.

Social support was associated with incident MCI/dementia, after adjusting for baseline age, ethnicity, race, HT trial arm, and history of HT use (tertile 3 vs. tertile 1: HR = 0.83, 95% CI 0.71–0.96; p_{trend} = 0.02; Table 3). After further adjustment for baseline education, income, history of diabetes, history of hypertension, and BMI, associations were slightly attenuated, but remained significant for tertile 3 vs. tertile 1 (HR = 0.85, 95% CI 0.74–0.99; p_{trend} = 0.08). Further adjustment for smoking and alcohol use in Model 3 did not materially change the associations (HR = 0.85, 95% CI 0.73–0.99; p_{trend} = 0.06). Associations were further attenuated and no longer significant after adjustment for depressive symptom severity (HR = 0.88, 95% CI 0.76–1.03; p_{trend} = 0.21). Associations were in the same direction, but weaker and not significant when examining MCI or dementia alone.

In analyses examining associations between MOS-SSS subscales and cognitive outcomes, significant inverse associations were observed for emotional/information support and positive social interaction in relation to incident MCI and MCI/dementia (Table 4). For both subscales, these associations were attenuated after adjustment for depressive symptoms in Model 4. Positive social interaction was associated with incident MCI (Model 1 tertile 3 vs. tertile 1: HR=0.81, 95% CI 0.67–0.97; p_{trend} = 0.06). Emotional/information support was associated with incident MCI/dementia (Model 1 tertile 3 vs. tertile 1: HR = 0.81, 95% CI 0.70–0.94; p_{trend}<0.01). Positive social interaction also was associated with incident MCI/dementia (Model 1 tertile 3 vs. tertile 1: HR = 0.81, 95% CI 0.70–0.94; p_{trend}<0.01). For emotional/information support and positive social interaction, results for tertile 3 vs. tertile 1 were attenuated after further adjustment for education, income, history of diabetes, history of hypertension, BMI, smoking and alcohol use, and were no longer significant after adjustment for depressive symptoms in Model 4 (both p_{trend}>0.10). Estimates for affection and tangible support subscales were not significant.

In sensitivity analyses, findings were similar using complete case analysis (Supplementary Tables 2 and 3) and after excluding women who were censored during the first two years or first 5 years of follow-up (Supplementary Tables 4–7). Hazard ratios were similar after applying IPCWs to account for selection bias due to censoring (Supplementary Tables 8 and 9). After stratifying analyses by Burnam scores, results were similar for those with no/minimal depressive symptom severity (i.e., Burnam scores   0.06) but were less precise among those with Burnam scores >0.06 due to reduced sample size (Supplementary Tables 10 and 11). Hazard ratios were similar after including marital status as a covariate in our primary analyses (Supplementary Tables 12 and 13). In analyses stratified by race, no significant associations were observed among Black women. However, the direction and magnitude of associations of perceived social support, emotional/information support, and positive social interaction were in the same direction and of similar magnitude in Models 1 and 2 among Black women compared to White women. Among Black women, but not among White women, adjustment for health behaviors attenuated the associations of perceived social support and emotional/information support (Supplementary Tables 14 and 15).

DISCUSSION

In this cohort study of 6,670 community-dwelling older women with an average 10.7 years of follow-up, greater perceived social support was associated with lower risk of incident MCI/dementia. Findings were attenuated slightly and no longer significant after adjustment for depressive symptom severity. We also observed significant associations for emotional/information support and positive social interaction with incident MCI/dementia. We observed that the highest, relative to the lowest, tertiles of social support had the strongest associations with incident MCI/dementia. However, clinically meaningful MOS-SSS categories have yet to be established.

A recent WHIMS and WHI Study of Cognitive Aging (WHISCA) study of 2,242 women found cross-sectional, but not longitudinal, associations between social support and cognitive function during a median six-year follow-up [24]. The current study extends these previous findings by using a larger analytic sample with longer follow-up to examine MCI and dementia, as well as four subscales of social support. Another study of 11,498 community-dwelling Australians aged 70 to 94 years found that low social support was associated with baseline cognitive function, but not cognitive decline and incident dementia [12]. A recent study of 4,514 participants from the Rotterdam Study and 2,112 participants from the Swedish National Study on Aging and Care in Kungsholmen found that loneliness, but not perceived social support, was associated with risk of dementia [13]. These divergent findings may be due to how social support was operationalized across studies as well as different sample sizes and follow-up time across studies, as well as differences in the characteristics of the study populations.

In the subscale analysis, emotional/information and positive social interaction subscales were associated with incident MCI/dementia. These results align with a cross-sectional study of 355 community-dwelling older adults that found both MOS-SSS subscales to be associated with cognition, as assessed by the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) [27]. Another longitudinal study of 493 older adults found that overall MOS-SSS and all subscales, except emotional/information support, were associated with incident RBANS decline over a median 4 years of follow-up [9]. However, neither study used rigorously adjudicated MCI and dementia outcomes and both had limited sample size, resulting in imprecise estimates. Further study is needed to determine whether these findings are applicable in larger study populations with extended follow-up.

Our observed associations were attenuated after adjustment for depressive symptoms, suggesting that this factor may mediate the relationship between social support and MCI/dementia. This is consistent with literature suggesting that social support is associated with lower risk of depression [28] and that depression may be a prodrome or symptom of dementia [29] as well as a potential modifiable risk factor for dementia [30]. However, we were underpowered to conduct a formal mediation analysis due to the small magnitudes of association for the total and controlled direct effects. After stratifying by Burnam scores, estimates among those with Burnam scores >0.06 had low precision, suggesting further study in large study samples.

Social support is likely one of many factors, such as social networks and relationships, that are associated with specific domains of cognitive health. For example, in the WHIMS and WHISCA study, social support was cross-sectionally associated with overall cognitive function, figural memory, verbal memory, and semantic fluency, but not with cognitive decline [24]. This aligns with a recent cross-sectional analysis that found that MOS-SSS and its subscales were associated with immediate and delayed recall memory among adults aged 45 to 85 years [31]. One systematic review found evidence to suggest associations between social support with global cognition and episodic memory, but not attention or processing speed [32]. More cohort studies are needed to better understand relations between social support subscales and cognitive trajectories.

There are substantial racial and ethnic disparities in dementia risk and prevalence [33,34], and risk and protective factors may differ by race and ethnicity [35]. Our study was under-powered to examine differences in associations by race and ethnicity. In stratified analyses, we observed some evidence of protective associations of higher perceived social support, emotional/information support, and positive social interaction among Black women, although associations were not significant, and may not be robust to adjustment for health behaviors. Studies with more diverse samples are needed to better understand the role of social support in MCI/dementia risk among individuals with different sociocultural backgrounds.

Our findings may support interventional strategies focused on improving social support as a potentially modifiable risk factor for MCI and dementia. While we found that emotional/information support and positive social interaction had the strongest associations, interventional studies are needed to confirm which aspects of social support have the most impactful cognitive benefit [32]. Even among those with dementia, social support-focused interventions have the potential to reduce depressive symptoms as well as improve quality of life and self-esteem [36–38].

This study has several limitations. First, given differential enrollment in WHIMS-ECHO, our results may have been prone to selection bias. Participant attrition may have also impacted selection bias. However, we addressed this bias by using stabilized IPCW and found similar results compared to unweighted models. Second, we examined social support at baseline and did not assess changes in levels of support over time. Further research is needed to assess the stability of social support over time and if time-varying factors would affect these associations [39]. Additionally, there is potential for reverse causation. However, results were similar after repeating primary analyses after excluding women who were lost to follow-up or developed cognitive outcomes during the first two years and first five years of follow-up. Lastly, our sample consisted primarily of older women who identified as White race and non-Hispanic/Latina ethnicity. Future work is needed to examine whether the observed associations differ in more racially and ethnically diverse populations, and whether they differ by sex [9,10].

Strengths of this study include the large sample size and prospective design with long term follow-up. Second, cognitive status was rigorously adjudicated, which may minimize any

influence of misclassification bias of MCI and dementia outcomes. Third, statistical models were able to account for many potentially confounding factors.

Among postmenopausal women, greater perceived social support, particularly the emotional/information and positive social interaction subscales, was associated with lower risk of incident MCI/dementia. However, our results were attenuated and not significant after adjustment for depressive symptom severity. Our findings suggest that increased surveillance for dementia may be warranted among older women with low levels of perceived social support. More research on the associations of other psychosocial factors, such as social isolation and loneliness, with cognitive outcomes are needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Medical Outcomes Study Social Support Survey (MOS-SSS) items and subscale components

MOS-SSS Item		Subscale
1	Someone you can count on to listen to you when you need to talk	Emotional/information support
2	Someone to give you good advice about a problem	Emotional/information support
3	Someone to take you to the doctor if you need it	Tangible support
4	Someone to have a good time with	Positive social interaction
5	Someone to help you understand a problem when you need it	Emotional/information support
6	Someone to help you with daily chores if you are sick	Tangible support
7	Someone to share your most private worries and fears	Emotional/information support
8	Someone to do something fun with	Positive social interaction
9	Someone to love you and make you feel wanted	Affection support

Notes: Participants were presented the following prompt, "People sometimes look to others for help, friendship, or other types of support. Next are some questions about the support that you have. How often is each of the following kinds of support available to you if you need it?" and then rated 9 MOS-SSS items to assess the amount of social support available to them. Responses to each item were rated on a five-point Likert scale: 1) None of the time; 2) A little of the time; 3) Some of the time; 4) Most of the time; and 5) All of the time.

Table 2.

Baseline characteristics by tertiles of perceived social support (N=6,670)

Characteristic		Tertiles (T) of perceived social support[a]			
		T1 (n=2,207)	T2 (n=2,318)	T3 (n=2,145)	p value
Social support	mean (SD)	26.54 (5.56)	37.07 (1.92)	43.59 (1.52)	
	median [range]	28 [9, 33]	37 [34.00, 40]	44 [41, 45]	
Age, mean (SD)		70.33 (3.913)	69.92 (3.810)	69.88 (3.711)	<0.01
Ethnicity, n (%)	Not Hispanic/Latina	2115 (95.83%)	2261 (97.54%)	2095 (97.67%)	<0.01
	Hispanic/Latina	81 (3.67%)	54 (2.33%)	41 (1.91%)	
	Unknown/Not reported	11 (0.50%)	3 (0.13%)	9 (0.42%)	
Race, n (%)	American Indian/Alaska Native	2 (0.09%)	6 (0.26%)	6 (0.28%)	0.02
	Asian	48 (2.18%)	36 (1.55%)	31 (1.45%)	
	Native Hawaiian/Other Pacific Islander	1 (0.05%)	3 (0.13%)	2 (0.09%)	
	Black	165 (7.48%)	159 (6.86%)	104 (4.85%)	
	White	1944 (88.08%)	2080 (89.73%)	1962 (91.47%)	
	More than one race	24 (1.09%)	18 (0.78%)	23 (1.07%)	
	Unknown/Not reported	23 (1.04%)	16 (0.69%)	17 (0.79%)	
HT trial arm, n (%)	E-alone intervention	453 (20.53%)	439 (18.94%)	407 (18.97%)	0.02
	E-alone control	474 (21.48%)	440 (18.98%)	392 (18.28%)	
	E+P intervention	633 (28.68%)	687 (29.64%)	673 (31.38%)	
	E+P control	647 (29.32%)	752 (32.44%)	673 (31.38%)	
Education, n (%)	High school or less	664 (30.14%)	652 (28.25%)	616 (28.80%)	0.20
	Some College	905 (41.08%)	934 (40.47%)	843 (39.41%)	
	College or greater	634 (28.78%)	722 (31.28%)	680 (31.79%)	
Income, n (%)	<$35,000	1353 (64.92%)	1237 (56.74%)	957 (47.61%)	<0.01
	>$35,000	731 (35.08%)	943 (43.26%)	1053 (52.39%)	
Marital status, n (%)	Never/divorced	500 (22.71%)	338 (14.59%)	194 (9.07%)	<0.01
	Widowed	897 (40.74%)	703 (30.35%)	425 (19.88%)	
	Married/ in relationship	805 (36.56%)	1275 (55.05%)	1519 (71.05%)	
BMI, mean (SD)		28.65 (5.83)	28.50 (5.60)	28.27 (5.60)	0.09
History of diabetes, n (%)	No	2050 (93.14%)	2195 (94.82%)	2030 (94.86%)	0.02

Characteristic		Tertiles (T) of perceived social support[a]			
		T1 (n=2,207)	T2 (n=2,318)	T3 (n=2,145)	p value
	Yes	151 (6.86%)	120 (5.18%)	110 (5.14%)	
History of hormone therapy, n (%)	Never used hormones	1138 (51.59%)	1286 (55.50%)	1204 (56.13%)	<0.01
	Past hormone user	942 (42.70%)	885 (38.20%)	783 (36.50%)	
	Current hormone user	126 (5.71%)	146 (6.30%)	158 (7.37%)	
History of hypertension, n (%)	No	984 (44.87%)	1109 (48.03%)	1042 (48.74%)	0.02
	Yes	1209 (55.13%)	1200 (51.97%)	1096 (51.26%)	
Smoking, n (%)	Never	1117 (51.50%)	1253 (54.79%)	1199 (56.40%)	<0.01
	Past	882 (40.66%)	881 (38.52%)	828 (38.95%)	
	Current	170 (7.84%)	153 (6.69%)	99 (4.66%)	
Alcohol intake, n (%)	Non-drinker	251 (11.48%)	315 (13.76%)	300 (14.04%)	<0.01
	Past drinker	471 (21.54%)	426 (18.60%)	370 (17.32%)	
	At least one drink in past month	1465 (66.99%)	1549 (67.64%)	1466 (68.63%)	
Depressive symptom severity, median (IQR)		0.0021 (0.020)	0.0017 (0.0020)	0.0014 (0.00038)	<0.01

[a] Social support is measured by the Medical Outcomes Study Social Support Survey (MOS-SSS); tertiles are uneven given tertile cutpoints based on distributional characteristics of the study population

Notes: BMI = body mass index, kg/m2; E = estrogen; HT = Hormone therapy; IQR= interquartile range; P = Progestin; SD =standard deviation. Missing data: education = 20 (0.3%); income = 395 (5.9%); marital status = 14 (0.2%); smoking = 88 (1.3%); alcohol intake = 57 (0.9%); history of diabetes = 14 (0.2%); history of hormone therapy = 2 (0.0%); history of hypertension = 2 (0.0%); history of hypertension = 30 (0.4%); depressive symptom severity = 186 (2.8%). Depressive symptom severity was measured using the Burnam algorithm.

Table 3.

Hazard ratios and 95% confidence intervals relating perceived social support to mild cognitive impairment (MCI), dementia, or either MCI/dementia from 1995–1999 to December 31, 2019

	MCI (n=6,226)	Dementia (n=6,170)	MCI/Dementia (n=6,670)
Events	753	697	1,197
Model 1			
Continuous	0.99 (0.98–1.00)	0.99 (0.98–1.00)	0.99 (0.98–1.00)
p for trend	0.18	0.24	0.02
T1	1.00 (ref)	1.00 (ref)	1.00 (ref)
T2	0.91 (0.77–1.08)	1.01 (0.84–1.21)	0.95 (0.83–1.10)
T3	0.85 (0.71–1.02)	0.88 (0.73–1.06)	0.83 (0.71–0.96)
Model 2			
Continuous	1.00 (0.99–1.01)	1.00 (0.99–1.01)	0.99 (0.99–1.00)
p for trend	0.38	0.40	0.08
T1	1.00 (ref)	1.00 (ref)	1.00 (ref)
T2	0.91 (0.77–1.08)	1.02 (0.85–1.23)	0.97 (0.85–1.12)
T3	0.88 (0.73–1.05)	0.90 (0.74–1.09)	0.85 (0.74–0.99)
Model 3			
Continuous	1.00 (0.99–1.01)	1.00 (0.99–1.01)	0.99 (0.98–1.00)
p for trend	0.36	0.55	0.06
T1	1.00 (ref)	1.00 (ref)	1.00 (ref)
T2	0.91 (0.76–1.08)	1.02 (0.85–1.23)	0.96 (0.83–1.10)
T3	0.86 (0.72–1.04)	0.92 (0.76–1.12)	0.85 (0.73–0.99)
Model 4			
Continuous	1.00 (0.99–1.01)	1.00 (0.99–1.01)	0.99 (0.99–1.00)
p for trend	0.74	0.83	0.21
T1	1.00 (ref)	1.00 (ref)	1.00 (ref)
T2	0.94 (0.79–1.12)	1.05 (0.87–1.26)	0.98 (0.85–1.14)
T3	0.90 (0.75–1.09)	0.95 (0.78–1.16)	0.88 (0.76–1.03)

Notes: MCI/Dementia includes incident MCI or dementia, whichever event was first. Tertiles (T) of perceived social support are defined as follows: T1=9–33, T2=34–40, T3=41–45. Model 1 includes continuous or tertiles of social support as the main exposure of interest and is adjusted for age (years), ethnicity (Not Hispanic/Latina; Hispanic/Latina/Unknown/Not reported), race (White; Black; American Indian/Alaska Native, Asian, Native Hawaiian/Other Pacific Islander, more than one race, unknown, or not reported), hormone therapy study arm (estrogen [E]-alone intervention; E-alone control;

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E+Progestin [P] intervention; E+P control), and history of hormone therapy (never; past; current). Model 2 includes Model 1 and adjusts for education (high school or less; some college; college or greater), income (<$35,000; >$35,000), history of diabetes (no; yes), history of hypertension (no; yes), and body mass index (kg/m2). Model 3 includes Model 2 and adjusts for smoking (never; past; current) and alcohol use (non-drinker; past drinker; at least one drink in the past month). Model 4 includes Model 3 and adjusts for depressive symptom severity as measured by the Burnam algorithm.

Table 4.

Hazard ratios and 95% confidence intervals relating Medical Outcomes Study Social Support Survey (MOS-SSS) subscales to mild cognitive impairment (MCI), dementia, or either MCI/dementia from 1995–1999 to December 31, 2019

MOS-SSS subscale	MCI (n=6,226)	Dementia (n=6,170)	MCI/Dementia (n=6,670)
Events	753	697	1,197
Emotional/information			
Model 1			
Continuous	0.99 (0.97–1.00)	0.98 (0.96–1.00)	0.98 (0.97–0.99)
p for trend	0.13	0.07	0.0084
T1	1.00 (ref)	1.00 (ref)	1.00 (ref)
T2	0.86 (0.72–1.02)	0.93 (0.77–1.12)	0.91 (0.79–1.04)
T3	0.84 (0.70–1.00)	0.82 (0.68–0.98)	0.81 (0.70–0.94)
Model 2			
Continuous	0.99 (0.97–1.01)	0.98 (0.97–1.00)	0.98 (0.97–1.00)
p for trend	0.27	0.13	0.04
T1	1.00 (ref)	1.00 (ref)	1.00 (ref)
T2	0.86 (0.72–1.03)	0.95 (0.79–1.14)	0.93 (0.80–1.07)
T3	0.86 (0.72–1.02)	0.83 (0.69–1.00)	0.84 (0.72–0.97)
Model 3			
Continuous	0.99 (0.97–1.01)	0.99 (0.97–1.01)	0.98 (0.97–1.00)
p for trend	0.27	0.17	0.03
T1	1.00 (ref)	1.00 (ref)	1.00 (ref)
T2	0.87 (0.72–1.03)	0.95 (0.79–1.15)	0.93 (0.80–1.08)
T3	0.86 (0.72–1.02)	0.85 (0.70–1.03)	0.83 (0.72–0.97)
Model 4			
Continuous	0.99 (0.98–1.01)	0.99 (0.97–1.01)	0.99 (0.97–1.00)
p for trend	0.54	0.30	0.11
T1	1.00 (ref)	1.00 (ref)	1.00 (ref)
T2	0.90 (0.75–1.07)	0.97 (0.80–1.17)	0.96 (0.83–1.11)
T3	0.89 (0.74–1.07)	0.87 (0.71–1.05)	0.86 (0.74–1.01)
Affection			

MOS-SSS subscale	MCI (n=6,226)	Dementia (n=6,170)	MCI/Dementia (n=6,670)
Model 1			
Continuous	0.99 (0.92–1.06)	0.98 (0.91–1.06)	0.96 (0.91–1.02)
p for trend	0.72	0.63	0.19
T1	1.00 (ref)	1.00 (ref)	1.00 (ref)
T2	1.07 (0.87–1.32)	1.18 (0.94–1.47)	1.11 (0.94–1.32)
T3	0.97 (0.81–1.17)	0.97 (0.79–1.19)	0.92 (0.79–1.08)
Model 2			
Continuous	1.00 (0.94–1.07)	0.99 (0.92–1.06)	0.97 (0.92–1.03)
p for trend	1.00	0.78	0.37
T1	1.00 (ref)	1.00 (ref)	1.00 (ref)
T2	1.09 (0.89–1.35)	1.19 (0.95–1.48)	1.13 (0.95–1.34)
T3	1.00 (0.83–1.21)	0.98 (0.80–1.21)	0.95 (0.81–1.11)
Model 3			
Continuous	1.00 (0.93–1.07)	1.00 (0.93–1.08)	0.97 (0.92–1.03)
p for trend	0.99	0.96	0.32
T1	1.00 (ref)	1.00 (ref)	1.00 (ref)
T2	1.10 (0.89–1.35)	1.17 (0.93–1.47)	1.10 (0.92–1.31)
T3	0.99 (0.82–1.20)	1.00 (0.81–1.23)	0.94 (0.80–1.10)
Model 4			
Continuous	1.02 (0.95–1.09)	1.01 (0.94–1.09)	0.99 (0.93–1.05)
p for trend	0.59	0.80	0.64
T1	1.00 (ref)	1.00 (ref)	1.00 (ref)
T2	1.13 (0.91–1.40)	1.19 (0.95–1.50)	1.12 (0.94–1.34)
T3	1.04 (0.86–1.27)	1.02 (0.83–1.27)	0.97 (0.83–1.15)
Tangible			
Model 1			
Continuous	1.00 (0.96–1.03)	1.00 (0.97–1.04)	0.99 (0.96–1.01)
p for trend	0.84	0.88	0.39
T1	1.00 (ref)	1.00 (ref)	1.00 (ref)
T2	1.00 (0.84–1.20)	1.04 (0.86–1.25)	1.00 (0.86–1.15)
T3	0.95 (0.79–1.13)	1.02 (0.85–1.23)	0.93 (0.81–1.07)

MOS-SSS subscale	MCI (n=6,226)	Dementia (n=6,170)	MCI/Dementia (n=6,670)
Model 2			
Continuous	1.00 (0.97–1.03)	1.01 (0.97–1.04)	0.99 (0.97–1.02)
p for trend	0.97	0.74	0.59
T1	1.00 (ref)	1.00 (ref)	1.00 (ref)
T2	0.98 (0.82–1.17)	1.04 (0.86–1.25)	1.00 (0.87–1.15)
T3	0.96 (0.80–1.15)	1.04 (0.86–1.25)	0.95 (0.82–1.10)
Model 3			
Continuous	1.00 (0.97–1.03)	1.01 (0.98–1.05)	0.99 (0.96–1.02)
p for trend	0.92	0.56	0.54
T1	1.00 (ref)	1.00 (ref)	1.00 (ref)
T2	1.00 (0.84–1.19)	1.05 (0.86–1.27)	0.99 (0.85–1.14)
T3	0.95 (0.79–1.14)	1.06 (0.87–1.28)	0.94 (0.81–1.09)
Model 4			
Continuous	1.01 (0.97–1.04)	1.02 (0.98–1.05)	1.00 (0.97–1.03)
p for trend	0.75	0.40	0.86
T1	1.00 (ref)	1.00 (ref)	1.00 (ref)
T2	1.03 (0.86–1.23)	1.07 (0.88–1.30)	1.01 (0.87–1.17)
T3	0.99 (0.82–1.19)	1.08 (0.89–1.32)	0.97 (0.83–1.13)
Positive social interaction			
Model 1			
Continuous	0.96 (0.93–1.00)	0.98 (0.94–1.02)	0.96 (0.93–0.99)
p for trend	0.06	0.34	0.0090
T1	1.00 (ref)	1.00 (ref)	1.00 (ref)
T2	0.91 (0.77–1.09)	0.94 (0.78–1.13)	0.93 (0.81–1.07)
T3	0.81 (0.67–0.97)	0.86 (0.71–1.04)	0.81 (0.70–0.94)
Model 2			
Continuous	0.97 (0.94–1.01)	0.99 (0.95–1.03)	0.97 (0.94–1.00)
p for trend	0.18	0.57	0.06
T1	1.00 (ref)	1.00 (ref)	1.00 (ref)
T2	0.92 (0.77–1.10)	0.96 (0.79–1.15)	0.96 (0.83–1.11)
T3	0.85 (0.70–1.02)	0.89 (0.73–1.08)	0.85 (0.73–0.99)

MOS-SSS subscale	MCI (n=6,226)	Dementia (n=6,170)	MCI/Dementia (n=6,670)
Model 3			
Continuous	0.97 (0.93–1.01)	0.99 (0.95–1.04)	0.96 (0.93–1.00)
p for trend	0.16	0.78	0.04
T1	1.00 (ref)	1.00 (ref)	1.00 (ref)
T2	0.91 (0.77–1.09)	0.94 (0.78–1.14)	0.93 (0.81–1.08)
T3	0.84 (0.70–1.01)	0.91 (0.74–1.10)	0.84 (0.72–0.97)
Model 4			
Continuous	0.98 (0.95–1.02)	1.00 (0.96–1.05)	0.98 (0.94–1.01)
p for trend	0.44	0.89	0.17
T1	1.00 (ref)	1.00 (ref)	1.00 (ref)
T2	0.95 (0.79–1.13)	0.97 (0.80–1.17)	0.97 (0.83–1.12)
T3	0.88 (0.73–1.06)	0.94 (0.76–1.14)	0.87 (0.74–1.02)

Notes: MCI/Dementia includes incident MCI or dementia, whichever event was first. Tertiles (T) of social support subscales were created in the overall cohort (n=6,670) and are defined as follows: Emotional/information, T1=4–14,T2=15–17,T3=18–20; Affection, T1=1–3,T2=4,T3=5; Tangible, T1=2–7,T2=8–9,T3=10; Positive social interaction, T1=2–7,T2=8–9,T3=9–10. Model 1 includes continuous or tertiles of social support as the main exposure of interest and is adjusted for age (years), ethnicity (Not Hispanic/Latina; Hispanic/Latina/Unknown/Not reported), race (White; Black; American Indian/Alaska Native, Asian, Native Hawaiian/Other Pacific Islander, more than one race, unknown, or not reported), hormone therapy study arm (estrogen [E]-alone intervention; E-alone control; E+Progestin [P] intervention; E+P control), and history of hormone therapy (never; past; current). Model 2 includes Model 1 and adjusts for education (high school or less; some college; college or greater), income (<$35,000; >$35,000), history of diabetes (no; yes), history of hypertension (no; yes), and body mass index (kg/m2). Model 3 includes Model 2 and adjusts for smoking (never; past; current) and alcohol use (non-drinker; past drinker; at least one drink in the past month). Model 4 includes Model 3 and adjusts for depressive symptom severity as measured by the Burnam algorithm.