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Psychiatric Disorders and Cognitive Dysfunction Among Older, Postmenopausal Women: Results From the Women's Health Initiative Memory Study

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Abstract

Objective—To estimate the frequency of depressive symptoms and selected psychiatric disorders in the Women's Health Initiative Memory Study (WHIMS) cohort and related them to cognitive syndromes.

Design—WHIMS was a randomized, double-blinded, placebo-controlled prevention clinical trial examining whether opposed and unopposed hormone therapy reduced the risk of dementia in healthy postmenopausal women. Participants scoring below a designated cutpoint on a cognitive screener received a comprehensive neuropsychiatric workup and adjudicated outcome of no cognitive impairment, mild cognitive impairment, or probable dementia.

Participants—Seven thousand four hundred seventy-nine WHIMS participants between age 65 and 79 years and free of dementia at the time of enrollment in WHIMS. Five hundred twenty-one unique participants contributed complete data required for these analyses.

Measures—Depressive symptoms were measured with the 15-item Geriatric Depression Scale and the presence of selected psychiatric disorders (major depression, generalized anxiety, and panic and alcohol abuse) was made using the PRIME-MD.

Results—The 18% of women had at least one psychiatric disorder with depression being the most common (16%) followed by general anxiety or panic (6%) and alcohol abuse (1%). Depression and the presence of a psychiatric disorder were associated with impaired cognitive status. Participants having a psychiatric disorder were more than twice as likely to be diagnosed with cognitive impairment as those with no psychiatric disorder (odds ratio = 2.06, 95% confidence interval = 1.17–3.60). Older age, white race, and diabetes were also associated with cognitive impairment.

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Conclusion—The frequency of a psychiatric disorder is associated with poorer cognitive functioning among older women enrolled in WHIMS. That approximately one in five women had a probable psychiatric disorder, most typically depression, highlights the need for greater detection and treatment efforts in this population.

Keywords

Psychiatric disorders; cognition; MCI; risk of dementia; comorbidity

Approximately one of every seven Americans older than 70 years suffers from some form of dementia.[1] Moreover, the prevalence of dementia increases significantly with age. Some form of dementia is present in approximately 1.5% adults at the age of 65 years[2] and rises to nearly 38% in those aged 90 years and older.[1] Discrete psychiatric disorders such as depression or other affective and anxiety disorders may cooccur with dementia.[3] The prevalence of clinically significant depression in patients with Alzheimer disease is between 20% and 25%.[4,5]

The occurrence of psychiatric comorbidities with mild cognitive impairment (MCI) or early dementia is an area of increasing interest, especially the relationship between depression and dementia.[6] Epidemiologic studies have been inconsistent, however. Early studies from France and the United States showed opposite findings. The French study failed to find an association with depressive symptoms and cognitive deterioration over a 3-year period,7 whereas the U.S. study found a twofold risk of incident dementia in persons with preexisting depression.8 Another study found that depressive symptoms predicted future cognitive losses in elderly persons with preexisting moderate cognitive impairment but did not find an association between depressive symptoms and onset or rate of decline for cognitively intact elderly.9 In contrast, the Monongahela Valley Independent Elders Survey demonstrated that depressive symptoms were cross-sectionally related to cognitive function but not associated with decline, and for those who developed dementia over time, baseline depressive symptoms did not exert much effect on decline.10 More recently, Chodosh et al.11 noted that from baseline to 7-year follow-up, higher levels of baseline depressive symptoms were associated with greater decline in cognitive performance among older adults aged 70–79 years at baseline. Finally, Becker et al.[12] found no consistent relationship between mood state and the development of dementia in subjects participating in the community-based cohort study, the Cardiovascular Health Study-Cognition (CHS-C).

The relationship between depression and the development of dementia is much stronger in clinical studies where patient diagnoses have been established, and it has been observed that patients with “reversible dementia” often fail to achieve a complete cognitive recovery after remission of depression and during follow-up. During follow-up, an average of 11%–23% of patients with an initially reversible dementia become irreversibly demented every year.[13–17]

The Women’s Health Initiative Memory Study (WHIMS),[18] a large, randomized, double-blinded, placebo-controlled prevention clinical trial, examined whether postmenopausal hormone therapy (HT) reduces the risk of all-cause dementia in healthy nondemented women aged 65–79 years at baseline. This study provides an opportunity to examine the association between depression and several psychiatric disorders and probable dementia (PD) and MCI. It is predicted that depression will be associated with diagnosed PD and MCI. It is also predicted that nondepressive disorders (anxiety, panic, and alcohol abuse) will also be associated with incident dementia and MCI, but the association will not be as strong as with depression. In addition, we will examine whether WHIMS treatment assignment or demographic or health variables are related to psychiatric morbidity.

METHODS

Sample

Participants for WHIMS were recruited during WHI HT trial from the estrogen plus progestin arm. Visits occurred annually for 7 years (1995–2002).[17] The 7,479 WHIMS participants were 65–79 years of age at baseline and free of PD as ascertained by the WHIMS protocol. Potential WHIMS participants were asked whether there were any reasons, such as serious emotional problems, mental illness, or too much stress, that would make it hard for them to be in a research study. Exclusion from the study based on these screening questions was thus strictly self-report. Furthermore, at the final eligibility assessment, the clinic staffs were asked to use their own judgment to determine whether the woman was ineligible based on depression. No other inclusion/exclusion criteria were required.

A detailed description of the WHIMS protocol for determining PD and MCI has been published.[17] Briefly, in Phase 1 of the WHIMS protocol, the participants received a cognitive screening with the Modified Mini-Mental State Examination (3MSE) at baseline and annually thereafter. Women advanced to Phase 2 of the protocol if they scored below an education-adjusted cutpoint on the 3MSE.[19,20] There were 521 women who advanced once or more to Phase 2.

Originally, the cut scores were ≤72 for those with ≤8 years of formal education and ≤76 for those with ≥9 years of education. However, to increase sensitivity, after 16 months new cutpoints of ≤80 for those with ≤8 years of education and ≤88 for those with ≥9 years of education were implemented. This resulted in an increase of 61 subjects that were included in the cohort of 521.

In Phase 2, women underwent a comprehensive neuropsychiatric examination that included the Consortium to Establish a Registry for Alzheimer's Disease battery of neuropsychological tests and standardized interviews of the participant and a proxy to assess acquired cognitive and behavioral impairments.[21,22] Phase 3 consisted of a clinical evaluation by a board-certified physician-specialist. The physician-specialist classified the WHIMS participant as having no cognitive impairment (NCI), MCI, or PD, based on *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, criteria.[23] All clinical and test data were then transmitted to the WHIMS CCC for review and central adjudication by a committee consisting of three board-certified specialists (two neurologists and one geriatric psychiatrist) with extensive experience in dementia.

Measures

Depressive Severity—Depressive symptom severity were assessed with the 15-item Geriatric Depression Scale (GDS).[24] Participants reporting ≥5 symptoms and ≥10 symptoms on the GDS were classified as depressed, and those with fewer symptoms were considered not depressed.

Psychiatric Diagnoses—The PRIME-MD psychiatric diagnostic interview[25] was administered by a trained and certified examiner and reviewed by the clinician to identify the following disorders: major depression, generalized anxiety, and panic and alcohol abuse. "Any depressive-anxiety-alcohol disorder" was a composite category created if women were classified as having at least one of the four psychiatric diagnoses. The PRIME-MD has been used with the elderly including those with cognitive impairment.[26–28] Screening instruments for bipolar disorders, thought disorders, personality disorders, or other substance abuse disorders were not used.

Panic Disorder—The panic symptoms list from the PRIME-MD includes 13 symptoms, so in addition to a categorical classification (panic disorder versus no panic disorder) a total symptom severity score which is the sum of the symptoms reported during the "last really bad time" an anxiety attack occurred during the past month.

Anxiety Disorder—The generalized anxiety scale includes six symptoms that have bothered the participant more than half the days during the last month. The score for the symptoms ranges from 0 to 6. A score <2 represents no anxiety. If the score is ≥2, the participant is then asked whether 1) the problems make it hard to do her work, take care of things at home, or get along with other people, 2) she has worried a great deal about different things, and 3) she has had all these problems for as long as 6 months. A positive answer to all three questions reflects probable generalized anxiety disorder. One of the three answers being negative reflects anxiety, not otherwise specified.

Alcohol Abuse Disorder—Alcohol abuse was determined with the participant answering a series of five questions on alcohol use. If any was answered positively, another series of five questions were asked about doctor's suggestion of a drinking problem, or drinking while working or taking care of others, or missing or being late at work because of drinking, or problems getting along with others while drinking, or driving a car after several drinks. If any of the questions from the second series was answered positively, the participant was identified with probable alcohol abuse/dependence. Otherwise, no alcohol problem is registered.

Analysis

All analyses were conducted at the Wake Forest University WHIMS Coordinating Center. Data were abstracted from the first below the cutpoint 3MS score. "On-trial" data from all 521 participants who received the full evaluation at least once after scoring below the cutpoint on the 3MSE were analyzed. Prevalence rates were compared between comparison groups using χ^2 or Fisher's exact tests. To further investigate the presence or absence of a disorder, logistic regression models were used to find the best fitting and most parsimonious model.[29] The response variable, a disorder, is a dichotomous outcome (yes or no). Adjustments for year of first below the cut-point 3MS score, age, and baseline 3MS scores were included in models for the two main outcomes, i.e., any depressive-anxiety-alcohol disorder and major depression. A multivariable logistic regression model was fitted to determine associations between psychiatric outcomes and cognitive outcomes and selected demographic and clinical factors. Parameters for the logistic models were estimated using standard maximum likelihood methods. The assessment of goodness of fit included computation and evaluation of overall measures based on residuals, e.g., the Pearson residual and the deviance residual.

RESULTS

During the course of the WHIMS clinical trial (N = 7,479), in total 971 neuropsychiatric evaluations were completed. Of these, 930 yielded a final diagnosis of NCI, MCI, or PD. Of these 891 evaluations, representing 521 unique participants, contributed complete data required for these analyses.

Table 1 includes the number of follow-up assessments at each annual visit. Missing data resulted from incomplete cognitive assessments because of various reasons including refusals, transportation issues, and other health problems. Twelve (2%) of the first abnormal 3MS scores occurred at baseline and none resulted in a PD diagnosis. The following percents of first abnormal 3MS scores occurred at subsequent visits: 23%, 30%, 16%, 13%, 9%, 5%, and 1% at years 1–7, respectively.

The prevalence of psychiatric morbidities at first abnormal 3MS score is presented in Table 2. The most common disorder was major depression affecting 84 (16%) participants. General anxiety or panic was diagnosed in 6% of the sample, whereas alcohol abuse was only found in 1%. Any depressive-anxiety-alcohol disorder was present in 93 (18%) women at first below the 3MS cutpoint score. None of these morbidities differed by treatment assignment to HT (data not shown).

The relationship between WHI baseline demographic, life style, and clinical characteristics and psychiatric morbidity status was examined (Table 3). The presence of any depressive-anxiety-alcohol disorder was associated with race ($p < 0.01$) with whites less likely to be affected than non-whites. Alcohol use was low overall and less common among those with any depressive-anxiety-alcohol disorder (28% versus 40%, $p = 0.02$). Those with any depressive-anxiety-alcohol disorder were more than twice as likely to have reported a history of diabetes (28% versus 13%, $p < 0.001$). There were no differences in these baseline characteristics by treatment assignment (data not shown).

A total of 239 (46%) participants were classified as NCI, 215 (41%) as MCI and 67 (13%) as PD. The cognitive groups were significantly different in relation to some psychiatric outcomes. Having any depressive-anxiety-alcohol disorder ($p < 0.01$) and having major depression ($p = 0.02$) were significantly associated with cognitive status. The MCI group was more likely to have major depression or any depressive-anxiety-alcohol disorder than the NCI group, significantly more likely to have major depression or any psychiatric morbidity than with the PD or NCI groups (Table 4). The number of women with depressive severity scores above the GDS cutpoint of 10 was greater among women judged to be cognitively impaired (MCI and PD) than women with NCI ($p = 0.03$), but the difference failed to reach statistical significance with conventional cutpoint of GDS = 5 ($p = 0.21$). Similar results were obtained after controlling for year of first abnormal 3MS score, age, and baseline 3MS scores for the presence of any depressive-anxiety-alcohol disorder and major depression.

As shown earlier, there were 282 participants classified with cognitive impairment (PD or MCI) at the time of their first abnormal 3MS score and neuropsychiatric evaluation. In addition, 38 other participants were subsequently classified with impairment at a later annual assessment. Therefore, we compared psychiatric comorbidities, at the time of first diagnosis, for those cognitively impaired versus those who remained nonimpaired, at the time of their last advancement to the neuropsychiatric evaluation (Table 5). The findings were similar to Table 4 even after adjusting for year of first 3MS score below cutpoint, age, and baseline 3MS scores. The cognitively impaired group experienced higher levels of depression, based on GDS cutpoints ≥ 5 and ≥ 10, and major depression ($p \leq 0.04$). Any depressive-anxiety-alcohol disorder also showed the same pattern ($p < 0.01$).

We determined the demographic, life style, and clinical factors associated with cognitive status at first neuropsychiatric evaluation, as a prelude to modeling cognitive impairment and its relationship to any depressive-anxiety-alcohol disorder. As described in Table 6, cognitively impaired women were significantly older ($p < 0.0001$), white ($p < 0.0001$), and had lower body mass index ($p = 0.04$).

The results of modeling the probability of cognitive impairment for women with or without any depressive-anxiety-alcohol disorder, based on multiple logistic regression, are presented in Table 7. We included covariates associated with cognitive impairment status (with $p < 0.20$ in Table 5), including age, education, race (white versus non-white), smoking, diabetes, body mass index, and baseline 3MSE and year of first neuropsychiatric evaluation. Assignment to HT was also included. After controlling for the covariates, the presence of any depressive-anxiety-alcohol disorder retained its association with cognitive impairment status ($p = 0.002$).

Those participants experiencing “any depressive-anxiety-depressive disorder” were more than twice as likely to be diagnosed with cognitive impairment as those not experiencing any morbidity (odds ratio = 2.06, 95% confidence interval = 1.35–3.60). Older women (p = 0.0001), whites (p = 0.02), and those with diabetes (p = 0.03) were also at elevated risk for cognitive impairment.

DISCUSSION

This study continues to add to the evidence that psychiatric morbidity, in particular depression, is significantly associated with PD and MCI in later life. Among WHIMS participants who screened positively for suspicious cognitive impairment “any psychiatric-anxiety-alcohol disorder” was present in one of five women, with depression as the most common disorder. Women with any depressive-anxiety-alcohol disorder were more likely to be non-white, less likely to consume alcohol, and had histories of diabetes. These rates are alarming and highlight the need for careful diagnosis and treatment of reversible morbidities such as depression and anxiety.

Any depressive-anxiety-alcohol disorder, and in particular depression, were significantly associated with being diagnosed with PD or MCI. The frequency of any depressive-anxiety-alcohol disorder and major depression in particular were about two times higher in the MCI group compared with women with no cognitive disorder and about 25% greater than women with PD. Our findings are consistent with other population-based studies.[10,30] However, they are at variance with those recently reported by Becker et al.[12] from the CHS-C. Both studies used large community-based samples, and similar screening instruments, screening instrument cutpoints, and approach to diagnostic adjudication. Although WHIMS used only women participants, CHS-C included both men and women, leading to the hypothesis, are women who are depressed at greater risk for developing cognitive impairment than men with depression?

In this study, there was a strong relationship between major depression and MCI. These findings are consistent from those originating from clinical populations. Apostolva and Cummings[31] have reported that the prevalence of behavioral symptoms associated with MCI, e.g., depression, anxiety, apathy, and irritability ranged from 35% to 75%. The classification of MCI has evolved a great deal since this study was begun. We defined MCI based on the generally accepted model at the time and did not subclassify subjects into amnestic, nonamnestic, or multiple domain types.[32] Of note, the amnestic subtype has been shown to be associated with a higher number of neuropsychiatric symptoms.[33] Could psychiatric disorders such as depression and anxiety contribute to this conversion? This question requires further study, especially in lieu of a recent population-based study comparing Chinese and U.K. subjects, which found that the relationship between depression and dementia might be temporal and only the most severe depressive cases of depression are risk factors for dementia.[34]

The multivariate analyses that modeled cognitive impairment among WHIMS subjects were also interesting. Those participants experiencing any depressive-anxiety-alcohol disorder were more than twice as likely to be diagnosed with cognitive impairment than those not experiencing any comorbidity. This is not likely attributable to mistaking depressive symptoms for cognitive symptoms as our adjudication criteria made diagnosing either PD or MCI more difficult if psychiatric symptoms were present. It was the strongest predictor of all demographic and clinical variables and even had a higher odds ratio than age. Our data suggest that having a psychiatric disorder, especially major depression, may be a risk factor for the development of a cognitive disorder. Given our concurrent assessment of cognitive and psychiatric disorders, we cannot confidently conclude causal direction. It is also possible that cognitive disorders are risk factors for psychiatric disorders. This finding further underscores the long-standing diagnostic recommendation that all patients who present with cognitive impairment should be

screened for psychiatric conditions, in particular depression. Interestingly, in these analyses, HT did not predict cognitive impairment.

Several limitations of this study must be considered. First, it is important to note that persons with certain self-reported mental illness were excluded from the WHI; therefore, the original cohort may not be representative of the population at large. Second, it should be noted that the No Psychiatric Disorder group was not a typical comparison condition in that they probably had elevated rates of depression/anxiety given that they failed the initial cognitive screen. This may have attenuated the differences between groups. Third, because women only received a complete evaluation if they registered a below cutpoint score on the 3MSE, our "normal" group may not be a truly normal sample but rather a group without clinically meaningful cognitive impairment.

Fourth, MCI as a diagnostic category has been continually refined since the enrollment of subjects in this study. We defined MCI based on the generally accepted model at the time and did not subclassify subjects into amnestic, nonamnestic, or multiple domain types.[32] Of note, the amnestic subtype has been shown to be associated with a higher number of neuropsychiatric symptoms.[33] Finally, the small number of cases can affect the variability of the psychiatric disorder prevalence estimates. However, for group comparisons, we used small sample statistical methods such as the Fisher's exact test when appropriate. Furthermore, for logistic regression analyses, we presented confidence intervals that provide information on the stability of the estimates.

In summary, study participants who showed suspicious cognitive impairment and were carefully evaluated and classified as having a cognitive disorder (PD and MCI), or not, nearly one in five had any depressive-anxiety-alcohol disorders, most frequently major depression. Having major depression was significantly associated with also receiving a diagnosis of PD or MCI even after controlling demographic and medical conditions. These data clearly highlight the importance of identifying psychiatric illnesses among older women with suspicious cognitive impairment even when detected by simple cognitive screeners. Underdetection and undertreatment of psychiatric morbidities are costly to individuals and to society.

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TABLE 1

Follow-Up Assessments of Women Entered into the WHIMS Cohort

Annual Visits	Number of Women Due Annual Assessments	Number of Assessments Completed (%)
1	521	494 (95)
2	521	488 (94)
3	518	481 (93)
4	506	438 (87)
5	363	295 (81)
6	208	164 (79)
7	65	40 (62)

Notes: Twenty-nine of the 521 women died during the course of the clinical trial. The completion rates for annual assessments for the 521 women were adjusted based on the date of death for those women who died during the year.

TABLE 2

Frequency of Psychiatric Comorbidities at First Phase 2 Neuropsychiatric Evaluation (N = 521)

Comorbidity (Number Missing)	Number (%)
GDS	
Cutpoint = 5	71 (14)
Cutpoint =10	17 (3)
Any depressive-anxiety-alcohol disorder[a] (14)	93 (18)
Major depression	84 (16)
General anxiety/panic (2)	29 (6)
General anxiety (2)	23 (4)
Panic	10 (2)
Alcohol abuse (13)	7 (1)

[a] Any depressive-anxiety-alcohol disorder includes major depression, general anxiety, panic, or alcohol abuse.

TABLE 3

Demographic, Lifestyle, and Clinical Factors for Participants by Any Depressive-Anxiety-Alcohol Disorder[a] at First Phase 2 Neuropsychiatric Evaluation

	Any Depressive-Anxiety-Alcohol Disorder, N (%)				
Factors	**No, N = 414**	**Yes, N = 93**	**χ^2 Value**	**Degrees of Freedom**	**p**
Age (years)					
65–69	120 (29)	25 (27)	5.14	2	0.08
70–74	151 (36)	45 (48)			
75+	143 (35)	23 (25)			
Education					
<High school	90 (22)	28 (30)	6.65	3	0.08
High school grad	94 (23)	24 (26)			
Some college	143 (35)	31 (33)			
College grad	86 (21)	10 (11)			
White	256 (62)	44 (47)	6.77	1	<0.01
Prior CVD	68 (16)	19 (20)	0.86	1	0.36
Hypertension					
None	181 (44)	29 (31)	5.51	2	0.07
Current/controlled	69 (17)	16 (17)			
Current/uncontrolled	164 (40)	48 (52)			
History of statin use	56 (14)	12 (13)	0.03	1	0.88
Baseline 3MSE					
<93	286 (69)	66 (71)	0.18	2	0.92
93–96	92 (22)	20 (22)			
97–100	36 (9)	7 (8)			
Alcohol use					
None	247 (60)	66 (72)	4.86	2	0.09
<1/day	142 (34)	21 (23)			
1 +/day	24 (6)	5 (5)			
History of smoking					
Never	234 (58)	57 (63)	1.77	2	0.42
Past	146 (36)	26 (29)			

Factors	Any Depressive-Anxiety-Alcohol Disorder, N (%)				
	No, N = 414	Yes, N = 93	χ^2 Value	Degrees of Freedom	p
Present	25 (6)	7 (8)			
History of diabetes	55 (13)	26 (28)	12.02	1	<0.001
BMI					
<25	131 (32)	27 (29)	3.22	3	0.36
25–29	143 (35)	29 (31)			
30–34	89 (22)	19 (20)			
35+	51 (12)	18 (19)			

[a] Any depressive-anxiety-alcohol disorder includes major depression, general anxiety, panic, or alcohol abuse.

TABLE 4

Psychiatric Comorbidities at First Phase 2 Neuropsychiatric Evaluation by Cognitive Status

Comorbidity (Number Missing)	Cognitive Status at First Evaluation, N (%)			χ^2 Value	Degrees of Freedom	p
	Probable Dementia, N = 67	MCI, N = 215	No Impairment N = 239			
GDS						
Cutpoint = 5	12 (18)	33 (15)	26 (11)	3.12	2	0.21
Cutpoint =10	5 (7)	9 (4)	3 (1)	7.38	2	0.03
Any depressive-anxiety-alcohol disorder[a] (14)	11 (16)	51 (25)	31 (13)	9.88	2	<0.01
Major depression	10 (15)	46 (21)	28 (12)	7.92	2	0.02
General anxiety/panic (2)	2 (3)	17 (8)	10 (4)	3.98	2	0.14
General anxiety (2)	2 (3)	13 (6)	8 (3)	2.34	2	0.32
Panic	0 (0)	7 (3)	3 (1)	Fisher's exact	—	0.20
Alcohol abuse (13)	0 (0)	5 (2)	2 (1)	Fisher's exact	—	0.31

[a] Any depressive-anxiety-alcohol disorder includes major depression, general anxiety, panic, or alcohol abuse.

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TABLE 5

Psychiatric Comorbidities for Participants at First Cognitive Impairment Versus Those Without Impairment at Last Neuropsychiatric Evaluation

Comorbidity (Number Missing)	Cognitive Status, N (%)		χ^2 Value	Degrees of Freedom	p
	Probable Dementia or MCI, N = 320	χ^2, N = 201			
GDS					
Cutpoint = 5	51 (16)	16 (8)	7.01	1	<0.01
Cutpoint =10	16 (5)	3 (1)	4.32	1	0.04
Any depressive-anxiety-alcohol disorder[a] (16)	71 (23)	23 (12)	9.75	1	<0.01
Major depression	64 (20)	21 (10)	8.25	1	<0.01
General anxiety/panic (2)	24 (8)	7 (3)	3.62	1	0.06
General anxiety (1)	17 (5)	6 (3)	1.60	1	0.21
Panic (1)	11 (3)	2 (1)	3.04	1	0.09
Alcohol abuse (15)	5 (2)	2 (1)	Fisher's Exact	—	0.72

[a] Any Depressive-Anxiety-Alcohol Disorder includes major depression, general anxiety, panic, or alcohol abuse.

TABLE 6

Demographic, Lifestyle, and Clinical Factors for Participants by Cognitive Status at First Neuropsychiatric Evaluation

Factor	Cognitive Status, N (%)		χ^2 Value	Degrees of Freedom	p
	Probable Dementia or MCI, N = 282	No Impairment N = 239			
Age (years)					
65–69	61 (22)	89 (37)	18.86	2	<0.0001
70–74	112 (40)	91 (38)			
75+	109 (39)	59 (25)			
Education					
<High school	59 (21)	61 (26)	5.59	3	0.14
High school grad	60 (21)	64 (27)			
Some college	106 (38)	72 (30)			
College grad	57 (20)	41 (17)			
White	195 (69)	117 (49)	21.49	1	<0.0001
Alcohol use					
None	169 (60)	151 (63)	1.05	2	0.60
<1/day	94 (33)	76 (32)			
1+/day	18 (6)	11 (4)			
History of smoking					
Never	169 (61)	132 (56)	5.52	2	0.07
Past	95 (35)	81 (35)			
Present	11 (4)	21 (9)			
Prior CVD	54 (19)	36 (15)	1.51	1	0.22
Hypertension					
None	114 (40)	102 (43)	1.07	2	0.59
Current/controlled	52 (18)	36 (15)			
Current/uncontrolled	116 (41)	101 (42)			
History of diabetes	50 (18)	32 (13)	1.93	1	0.17
History of statin use	37 (13)	32 (13)	0.01	1	0.93
BMI					
<25	98 (35)	66 (28)	8.30	3	0.04

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Factor	Cognitive Status, N (%)		χ^2 Value	Degrees of Freedom	p
	Probable Dementia or MCI, N = 282	No Impairment N = 239			
25–29	96 (34)	79 (33)			
30–34	60 (21)	51 (21)			
35+	28 (10)	43 (18)			
Baseline 3MSE					
<93	184 (65)	177 (74)	5.89	2	0.06
93–96	68 (24)	48 (20)			
97–100	30 (11)	14 (6)			
Year of first neuropsychiatric evaluation					
Baseline	12 (5)	0 (0)	39.66	7	<0.0001
1	72 (30)	50 (18)			
2	79 (33)	79 (28)			
3	30 (13)	55 (20)			
4	24 (10)	44 (16)			
5	13 (5)	33 (12)			
6	8 (3)	17 (6)			
7	1 (0)	4 (1)			

TABLE 7

Likelihood of First Diagnosis of Cognitive Impairment (Probable Dementia or Minor Cognitive Impairment) as Associated With Selected Demographic and Clinical Factors: Results of Multivariable Logistic Regression Modeling, Controlling for Year of First Neuropsychiatric Evaluation

Factors	Odds Ratio	95% CI	p
Age	1.12	1.05–1.18	0.0001
Education			0.92
College grad (reference)			
Some college	0.85	0.48–1.53	
High school grad	0.81	0.43–1.54	
Less than high school	0.82	0.43–1.57	
Race			0.02
Non-white (reference)			
White	1.80	1.15–2.84	
Smoking			0.75
Never (reference)			
Past	0.93	0.60–1.43	
Current	0.74	0.33–1.66	
Diabetes	1.98	1.09–3.59	0.03
BMI	0.99	0.96–1.03	0.75
Baseline 3MSE	0.96	0.93–1.00	0.08
Hormone therapy	0.86	0.57–1.29	0.47
Any depressive-anxiety-alcohol disorder[a]	2.06	1.17–3.60	0.02

Notes: p values are from Wald χ^2 test with $df = 1$.

[a] Any depressive-anxiety-alcohol disorder includes major depression, general anxiety, panic, or alcohol abuse.