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Authors

Dhana, Anisa

DeCarli, Charles S

Dhana, Klodian

et al.

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Cardiovascular Health and Cognitive Outcomes: Findings from a Biracial Population-based Study in the United States

Anisa Dhana, MD MSc[1,2], **Charles S. DeCarli, MD**[3], **Klodian Dhana, MD PhD**[1,2], **Pankaja Desai, PhD**[1,2], **Thomas M. Holland, MD MSc**[1,2], **Denis A. Evans, MD**[1,2], **Kumar B. Rajan, PhD**[1,2,3]

[1] Rush Institute for Healthy Aging, Rush University Medical Center, Chicago, IL 60612.

[2] Department of Internal Medicine, Rush University Medical Center, Chicago, IL 60612.

[3] Department of Neurology, University of California at Davis, Sacramento, CA 95817.

Abstract

INTRODUCTION: To evaluate the association of cardiovascular health (CVH) with cognitive outcomes, including incident Alzheimer's dementia, rate of cognitive decline, and measures of brain injury and structure.

METHODS: This study consisted of 1,702 Black or African American and White participants living in the south side of Chicago, Illinois, and enrolled in the Chicago Health and Aging Project, a population-based cohort since 1993. CVH was based on seven risk factors, including diet, physical activity, body mass index, smoking, dyslipidemia, hypertension, and diabetes.

RESULTS: In a multivariable-adjusted model, CVH was associated with a lower risk of Alzheimer's dementia. The hazard ratio per one additional point in CVH score was 0.84 (95%CI 0.76, 0.94). CVH was also associated with a slower rate of cognitive decline and less volume (injury) in white matter hyperintensities.

DISCUSSION: Promoting CVH in communities with Black residents may lower the future risk of Alzheimer's dementia.

Keywords

Cardiovascular Health; Incidence; Alzheimer's disease; Dementia; Cognition; MRI; White Matter Hyperintensities; Epidemiology

Corresponding Author Anisa Dhana, MD, MSc, Postdoctoral Researcher, Rush University Medical Center, 1700 W Van Buren, Suite 245, Chicago, IL 60612, Phone: +1 (312) 942-3350, anisa_dhana@rush.edu.

Conflicts

CSD, KD, and KBR are funded by NIH research grants and reports no conflicts of interest. AD, PD, TMH, and DAE reports no conflicts of interest.

Consent Statement

The Institutional Review Board of the Rush University Medical Center approved the CHAP study protocols, and all participants provided written consent for population interviews, blood collection, and clinical evaluations.

Background

Alzheimer's dementia – a progressive neurological disease affecting cognitive abilities that interferes with daily functioning – is attributed to the co-occurrence and complex interactions among multiple risk factors, including age, genetics, environment, vascular, and lifestyle [1–5]. Recognizing the impact of dementia on daily life activities in older adults and their caregivers, together with the socioeconomic burden on our society, the World Health Organization, G8 Dementia Summit, and National Alzheimer's Project Act have all agreed that primary prevention of Alzheimer's dementia is a high priority for public health worldwide. [6,7].

Historically public health organizations have successfully reduced the risk of diseases through primary prevention; for instance, the rates of cardiovascular disease declined significantly in the latter part of the 20th century due to improvements in cardiovascular risk factors [8]. More recently, the American Heart Association has developed a cardiovascular health metric, Life's Simple 7, to monitor and prevent cardiovascular disease. Life's Simple 7 includes four behavioral factors (physical activity, diet, smoking, and body mass index) and three health factors (dyslipidemia, hypertension, and diabetes) [9]. Owning that cardiovascular disease and dementia often co-exist, as it is shown that 80% of individuals with Alzheimer's dementia show vascular pathology at autopsy [10,11], suggests that primary prevention of cardiovascular disease may contribute to lower the risk of Alzheimer's dementia. Numerous studies have shown that an optimal cardiovascular health level is associated with a lower risk of dementia [12–20]. However, most of these findings originate from analyses that include primarily whites, while there is a significant racial disparity in cardiovascular risk factors, with African Americans more likely to be affected by obesity, diabetes, dyslipidemia, and hypertension than non-Hispanic whites [21].

Therefore, we utilized data from a biracial cohort study in the south side of Chicago to evaluate the association of cardiovascular health (CVH) with the risk of Alzheimer's dementia. In addition, we sought to develop the trajectories of global cognition over 18 years of follow-up, according to the CVH level. We also sought to investigate the relationship between CVH, white matter hyperintensities, hippocampus, and grey matter volume assessed through magnetic resonance imaging (MRI) scans.

Methods

Study Design and Population

We conducted the study within the Chicago Health and Aging Project (CHAP), a population-based cohort study comprised of Black or African Americans and white adults 65 years or older living in the south side of Chicago, Illinois. The objectives and design of CHAP have been described previously in detail [22,23]. In short, CHAP was initiated in 1993 with an enrollment of 6,157 participants based on a door-to-door census. Successive cohorts recruited an additional 4,645 age-eligible participants living in the study area. In total, CHAP enrolled 10,802 participants from 1993 to 2012. Data, including cognitive assessment, were acquired for all participants during in-home visits (i.e., population interview) through structured self or interviewer-administered questionnaires

every 3 years up to 6 times throughout the study period. In addition, at each of these assessments, a stratified random sample was selected for an extended clinical evaluation to determine the prevalence and incidence of clinical Alzheimer's dementia [23]. The stratified random sample was based on age, sex, race, and categories of cognitive function of the study population [23]. For the stratified random sample, individuals were defined without Alzheimer's dementia at the baseline if they had good cognitive function during the population interview or if extended clinical evaluation indicated no cognitive impairment to indicate the presence of dementia [23]. Individuals without dementia at baseline were examined for the incidence of Alzheimer's dementia during the follow-up. From 1993 to 2012, 2,794 participants underwent detailed clinical evaluation for the prevalence and incidence of Alzheimer's dementia. Additional details on the sampling and clinical examination for Alzheimer's dementia are provided in early and recent publications [5,23].

For the present study, we focused on participants evaluated for the incidence of Alzheimer's dementia (n=2,130). Of 2,130 participants, we excluded those without data (n=369) on the factors included in the CVH (i.e., Life Simple 7). Among 1,761 remaining participants, we excluded those without genetic data [i.e., Apolipoprotein E (APOE)] or missings in other covariates (n=59). Our study population comprised 1,702 participants Supplementary Figure 1. We compared the demographics of our study population (n=1,702) with participants evaluated for the incidence of Alzheimer's dementia (n=2,130). We found no differences in age, sex, race, and education at the baseline (Supplementary Table 1).

Cardiovascular Health (CVH) Score

The CVH score was based on Life's Simple 7 definitions published by the American Heart Association [9]. We adopted definitions for dyslipidemia and diabetes components based on data available in CHAP, as described in Supplementary Table 2. According to American Heart Association, a healthy diet comprises five components, consuming fruits and vegetables, fish, whole grains and reducing sodium and sugar-sweetened beverages. We obtained dietary information from a validated 144-item food frequency questionnaire [24]. Physical activity levels were assessed via the 1985 US Health Interview Survey. They included moderate or vigorous activities, i.e., walking for exercise, gardening or yard work, calisthenics or general exercise, bicycle riding, and swimming. Smoking status was self-reported as never, current, and former smokers [25]. Body mass index was calculated as weight in kilograms divided by height in square meters and classified into three categories, normal weight <25m/kg2, overweight 25–30m/kg2, and obese >=30m/kg2. Systolic and diastolic blood pressure was measured by trained staff during home interviews. Diabetes and dyslipidemia status were determined based on self-report or medication use. During the home interview, trained research staff asked the study participant whether the doctor had ever told them they had diabetes, sugar in the urine, or high blood sugar. In addition, research staff objectively assessed and noted the participant's medication use. Metformin or insulin use implied diabetes diagnosis. Statin medication indicated dyslipidemia.

Based on the literature, we assigned a score of 0, 1, or 2 for each participant based on the adherence or status of the seven cardiovascular health factors (Supplementary Table 2) [9,15]. The scores for each factor were then summated to create a total score reflecting the

overall CVH. The CVH score ranged from 0 to 14, with a higher score suggesting better cardiovascular health.

Covariates

Demographic variables including race, sex, and education were assessed using the 1990 US census questions. Genotyping using the hME Sequenom MassARRAY platform determined whether study participants were APOE e4 carriers (i.e.,>=1 e4 allele) or noncarriers. History of heart disease and stroke was determined by self-report questions from the Established Populations for the Epidemiologic Study of the Elderly. Late-life cognitive activity is a composite measure, ranging from 1 to 5, of participation in cognitively stimulating activities, including reading, writing letters, visiting a library, and playing games such as chess or checkers [26]. Depressive symptoms were assessed with a modified 10-item version of the Center for Epidemiologic Studies Depression (CESD) scale [27].

Clinical Diagnosis of Alzheimer's Dementia

Clinical diagnosis of Alzheimer's dementia was determined using data from a structured neurologic examination, medical history, and cognitive testing for five domains, orientation, attention, memory, language, and perception. With an algorithmically based cognitive impairment rating, a board-certified neuropsychologist and neurologist determined the diagnosis of Alzheimer's dementia based on criteria of the joint working group of the National Institute of Neurologic and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS and ADRDA) for probable Alzheimer's disease [28]. A clinical diagnosis of incident Alzheimer's dementia was performed from 1993 until February 2012.

Global Cognition

During in-home population assessments, four cognitive tests were administered to all participants [29]. We computed the global measure of cognitive function by averaging four cognitive tests – two tests of episodic memory, one test of executive function, and the MMSE, after centering and scaling each to the baseline mean and standard deviation of the original cohort [30–32]. Cognitive tests were administered every three years up to six times (average 4.3 for the current sample) throughout the study, allowing us to develop trajectories of global cognition over 18 years of the study period [33].

Structural MRI Evaluations

From 2000 to 2012, participants with a clinical evaluation for Alzheimer's dementia were invited to participate in the MRI study. Individuals who agreed to participate in the MRI study were scanned at the High-Tech Imaging Center, Palos Heights, IL using the same General Electric 1.5T scanner (Excite platform, version 11; General Electric Healthcare, Milwaukee, Wisconsin) [34,35]. The scans were digitally transferred to the Imaging of Dementia and Aging Laboratory at UC Davis for processing and analysis. White matter hyperintensity was assessed on a combination of fluid-attenuated inversion recovery and 3-dimensional T1 MRI scans using a modified Bayesian probability structure based on a previously published method of histogram fitting. Hippocampal and grey matter

volumes were assessed by a multi-atlas hippocampal segmentation algorithm. Volumes were corrected for intracranial volume, multiplied by 1000, and log10-transformed to normalize the data.[36] Of 1,702 participants in our study, 671 had data on white matter hyperintensity, hippocampal, and grey matter volumes. Compared to participants without MRI data (n=1031), those with MRI evaluation (n=671) were, on average, younger (71.5 vs. 74.0 years old) and had a slightly higher education (13.3 vs. 12.8 years of formal schooling). Also, the MRI sample comprised more African American people (60% vs 49%). These MRI scans were for research purposes [37].

Statistical Analysis

The association between CVH and incident Alzheimer's dementia was evaluated using weighted Cox proportional hazard models. The CVH score was evaluated as a continuous variable per 1-point increase in the CVH score and as a categorical variable. For categorical analyses, we grouped participants into three classes, those with CVH score from 0 to 6, 7 to 9, and 10 to 14, and the reference category were people with CVH scores ranging from 0 to 6. As a sensitivity analysis, we also evaluated the relationship of CVH in tertiles (e.g., third and second tertile v.s. first tertile) with the incidence of Alzheimer's dementia. Models were adjusted by age (years), sex (men and women), race (African Americans and non-Hispanic whites), APOE e4 (with and without e4 allele), cognitive activities (score 1 to 5), education (years of formal schooling), cardiovascular disease (heart disease or stroke, or none), and CESD depression symptoms (score 1 to 10). The proportional hazard assumption was assessed by interacting with time and Schoenfeld residuals. Interactions between CVH score with sex, race, and APOE e4 carrier status on the risk of dementia were evaluated. However, we prespecified to conduct analyses separately for men and women, African Americans and whites, and carriers and non-carriers of the APOE e4 allele.

Trajectories of global cognition across 18 years of follow-up according to CVH categories were developed using linear mixed models. The models included an intercept referring to global cognition at baseline and time and corresponding random effects to account for interindividual variability. Models were adjusted by age, sex, race, APOE e4, cognitive activities, education, cardiovascular disease, CESD depression symptoms and follow-up time. We estimated the annual longitudinal change in cognitive function.

Linear regression analysis was used to investigate the association between CVH score, white matter hyperintensities, hippocampal volume, and grey matter in a multivariable model adjusted for age, sex, race, education, and APOE e4. In addition, we computed the lag between CVH and MRI assessments and adjusted the multivariable model to account for the time gap between these assessments.

Analyses were conducted using the R program and a set of set of R packages, version 4.1 (R Group for Statistical Computing) [38]. Our a priori cutoff for statistical significance included $P<0.05$. Hypothesis tests were 2-sided.

Results

Table 1 shows the demographic and clinical characteristics of the overall study population and stratified by the CVH categories. The average age of the study population was 73 years, 62% were women, and 53% were African Americans. About 31% of participants were carriers of at least one APOE e4 allele. African American participants comprised the majority (71.5%) of people with CVH score ranging from 0 to 6 points. The average years of formal schooling in people with CVH score 0 to 6 was 12.3 years. Among people with CVH score of 10 to 14 points, 67.3% were whites, and the average education was 13.7 years. Supplementary Figure 2 shows the distribution of CVH scores in African American and white participants. African American participants had a lower CVH score compared to white individuals.

Cardiovascular Health (CVH) and Alzheimer's Dementia

Table 2 shows the association of CVH score with incident Alzheimer's dementia. During 14,227 person-years of follow-up, 351 individuals developed incident Alzheimer's dementia. In a multivariable model, per 1 additional point in the CVH score, the hazard ratio (HR) and 95% confidence interval (CI) were 0.85 (95%CI 0.77, 0.94). In addition, compared to individuals with a CVH score of 0 to 6 points, the HRs (95%CI) in those with 7 to 9 and 10 to 14 points were 0.45 (95%CI 0.29, 0.70) and 0.39 (95%CI 0.23, 0.68), respectively. We also investigated the relationship of CVH score in tertiles with incident Alzheimer's dementia and found similar results (Supplementary Table 3).

Table 3 shows the association of CVH score (per 1-point increase) with incident Alzheimer's dementia stratified by sex, race, education, APOE e4 carrier status, and presence of cardiovascular disease. In multivariable models, per 1 additional point in CVH score, the HRs (95%CIs) of Alzheimer's dementia were 0.84 (0.7, 1.00) for men, 0.85 (0.75, 0.96) for women, 0.84 (0.74, 0.96) for African American and 0.84 (0.71, 0.99) for white older adults. CVH was also associated with a lower risk of Alzheimer's dementia in people with and without APOE e4, HR 0.87 (95%CI 0.75, 1.01) and HR 0.83 (95%CI 0.72, 0.95), respectively. The non-differential relationship across sex, race, and APOE e4 was also confirmed by a non-significant interaction term (P-value > 0.43) in Cox proportional hazard models.

Cardiovascular Health (CVH) and Trajectories of Global Cognition

Figure 1 shows the trajectories of global cognition during 18 years of study according to CVH categories. Individuals with a CVH score ranging from 0 to 6 points had an annual rate of cognitive decline of −0.049 (95%CI −0.059, −0.039), those with 7–9 points −0.041 (95%CI −0.049, −0.034), and those with 10–14 points −0.034 (95%CI −0.042, −0.025). Compared to individuals with a CVH score of 0 to 6 points, those with 7–9 and 10–14 points had a slower annual rate of cognitive decline by 0.008 (95%CI −0.001, 0.018) and 0.015 (95%CI 0.004, 0.026) standard deviation units, respectively.

Cardiovascular Health (CVH) and MRI measures

Table 4 shows the association of CVH with white matter hyperintensity, hippocampus, and grey matter volume. In the multivariable-adjusted model, one additional point in CVH score was associated with 0.028 log10 transformed unit less white matter hyperintensity volumes (β −0.028; 95%CI −0.050, −0.005). Compared to individuals with CVH score of 0 to 6 points, those with 7–9 and 10–14 points had −0.134 (95%CI −0.242, −0.026) and −0.142 (95%CI −0.272, −0.012) less white matter hyperintensity volumes, respectively. CVH was also associated with gray matter volumes [β for a 1-point increase: 0.002 (95%CI 0.001, 0.004)] but not with the hippocampal volume (β; 0.001; 95%CI −0.001, 0.003).

Discussion

In this prospective cohort study of Black or African American and white adults living in the southside of Chicago, Illinois, aged 65 and older, the CVH score defined by the American Heart Association (i.e., Life Simple 7 [9]) was associated with a lower risk of Alzheimer's dementia. In addition, individuals with higher CVH scores had a slower rate of cognitive decline during the 18 years of the study period and less white matter hyperintensity volume, a marker of cerebrovascular disease. Although the distribution of CVH scores varied by race –white individuals had better CVH than African American adults– the association between CVH and incident Alzheimer's dementia was similar across races.

The association between CVH and the risk of dementia has been reported previously [12–20], herein we complement these findings with data on incident Alzheimer's dementia, trajectories of cognitive decline, and markers of brain health. An earlier study from cohort data in France (i.e., Three-City Study), including individuals aged 65 years or older, showed that the incidence rates of dementia decreased with the increasing number in CVH metrics [14]. Another European study (Whitehall II) that recruited study participants from the British civil service in 1985–88, aged 35–55, showed that CVH at age 50 was associated with a lower risk of dementia later in life [15]. Similar findings are reported from studies conducted in the United States. For example, data from the Framingham Heart Study Offspring cohort [13], Atherosclerosis Risk in Communities Study [18], The Reasons for Geographic And Racial Differences in Stroke Study [12], and Washington Heights-Inwood Columbia Aging Project study [17] showed that higher CVH scores were associated with lower risk of dementia. While our results align with prior findings among Americans, we advance these findings with a diagnosis of incident Alzheimer's dementia based on criteria of NINCDS and ADRDA. In addition, we complemented our primary findings with data on trajectories of global cognition over 18 years of the study period and markers of brain structure and cerebrovascular disease (i.e., white matter hyperintensities).

Our study, also investigated how the CVH score was distributed in African American and white individuals. We found that African American individuals had lower adherence to behavioral and health factors than their white counterparts. It is well-documented that there is a significant racial disparity in cardiovascular risk factors, with high rates of obesity, diabetes, dyslipidemia, and hypertension in African Americans [21]. Comparable distributions were shown in similar studies from Atherosclerosis Risk in Communities Study [18], The Reasons for Geographic And Racial Differences in Stroke Study [12],

and Washington Heights-Inwood Columbia Aging Project [17]. However, although these differences in the distribution of CVH in African American and white participants, higher CVH score was associated with a lower risk of Alzheimer's dementia in both races – these findings align with previous literature [12,17,18].

American Heart Associated developed the cardiovascular health score (i.e., Life Simple 7) to prevent cardiovascular disease (i.e., heart disease and stroke); nevertheless, we and others showed that it might help prevent Alzheimer's dementia, suggesting that the heart and brain share similar risk factors [10,11]. To explore potential mechanisms by which cardiovascular health (CVH) is associated with a low risk of Alzheimer's dementia, we dedicated an analysis to the association of CVH with brain structure as measured by volumes of white matter hyperintensities and hippocampus. We found CVH was associated with white matter hyperintensities. These data suggest that the mechanistic pathway of CVH on dementia risk is partly through vascular pathology [39].

Our study has several limitations which should be acknowledged. First, the components of CVH, including dietary intake, physical activity, and smoking history, are based on self-report, which is prone to misclassification, although these questionnaires were validated [24]. In addition, the diagnosis of diabetes was, in part, self-reported. Second, CVH was determined at the baseline, and we did not investigate the possibility of changing during the follow-up. Third, findings are based on African American and white older adults living in the southside of Chicago, limiting the generalizability to younger populations and other ethnicities (e.g., Hispanics). The results of this study should be replicated in other study populations. Strengths of this study include the frequency of neuropsychological testing and structured clinical neurologic evaluations by clinicians to accurately diagnose Alzheimer's dementia. Several components of CVH, including systolic and diastolic blood pressure, BMI, and data on medication use for hypertension diagnosis, dyslipidemia, and diabetes, were determined by qualified research staff.

In conclusion, our study suggests that CVH is essential for cognitive health in older adults. Encouraging public health policies to promote better CVH (e.g., Life Simple 7) in communities with African American residents may lower the risk of Alzheimer's dementia in the future.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Research in Context

Systematic Review:

The cardiovascular health index (i.e., Life Simple 7), developed by the American Heart Association (AHA) to assess and monitor cardiovascular disease risk, has been associated with dementia risk. However, most studies originate from populations comprised of primarily white participants.

Interpretation:

Cardiovascular health score was similarly associated with a lower risk of Alzheimer's dementia in Black and White individuals. We also found that cardiovascular health score was associated with less volume in white matter hyperintensities and greater grey matter volumes.

Future Directions:

This study suggests cardiovascular health is essential for cognitive health in older adults. Public health programs, which include screening and promoting cardiovascular health through Life Simple 7 in communities with Black residents, may help to lower the risk of Alzheimer's dementia in the future.

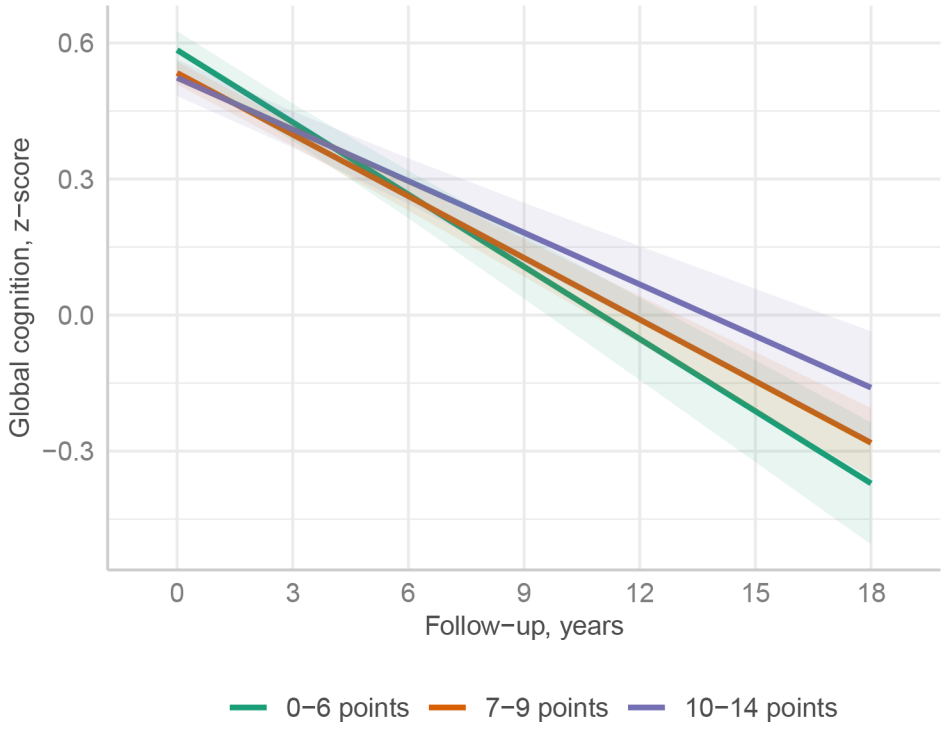

Figure 1: Trajectories of global cognition during 18-years of study

Individuals with a CVH score ranging from 0 to 6 points had an annual rate of cognitive decline of −0.049 (95%CI −0.059, −0.039), those with 7–9 points −0.041 (95%CI −0.049, −0.034), and those with 10–14 points −0.034 (95%CI −0.042, −0.025). Compared to individuals with a CVH score of 0 to 6 points, those with 7–9 and 10–14 points had a slower annual rate of cognitive decline by 0.008 (95%CI −0.001, 0.018) and 0.015 (95%CI 0.004, 0.026) standard deviation units, respectively.

Table 1.

Demographic and clinical characteristics of the study population and stratified by the cardiovascular health score

		Cardiovascular Health Score		
Variables	**Overall**	**0–6**	**7–9**	**10–14**
n	1702	368	946	388
Age, years mean (SD)	73.0 (5.8)	71.9 (5.4)	73.2 (5.7)	73.9 (6.0)
Sex, men, n (%)	653 (38.4)	125 (34.0)	398 (42.1)	130 (33.5)
Race, Blacks or African Americans, n (%)	906 (53.2)	263 (71.5)	516 (54.5)	127 (32.7)
APOE e4 allele, n (%)	540 (31.7)	120 (32.6)	298 (31.5)	122 (31.4)
Education, years, mean (SD)	13.0 (3.4)	12.3 (3.2)	12.9 (3.3)	13.8 (3.4)
Cognitive activities, mean (SD)	3.3 (0.6)	3.2 (0.6)	3.3 (0.6)	3.4 (0.5)
Cardiovascular disease, n (%)	274 (16.1)	77 (20.9)	152 (16.1)	45 (11.6)
CESD depression score, mean (SD)	1.4 (1.8)	1.7 (2.0)	1.3 (1.7)	1.1 (1.6)
Body mass index, kg/m2, mean (SD)	27.5 (5.3)	30.7 (5.4)	27.6 (5.1)	24.4 (3.4)
Diet score*, mean (SD)	1.0 (0.9)	0.7 (0.7)	0.9 (0.8)	1.3 (1.0)
Physical activity, minutes/week, median [interquartile]	105.0 [5.0, 280.0]	0.0 [0.0, 68.1]	100.0 [13.5, 261.9]	240.0 [148.1, 435.0]
Current smoking, n (%)	207 (12.2)	87 (23.6)	111 (11.7)	9 (2.3)
Systolic blood pressure, mmHg, mean (SD)	138.7 (19.2)	145.3 (19.6)	139.4 (18.5)	130.6 (17.5)
Diastolic blood pressure, mmHg, mean (SD)	77.3 (10.6)	79.2 (11.4)	77.8 (10.4)	74.1 (9.6)
Antihypertensive drug use, n (%)	962 (56.5)	274 (74.5)	540 (57.1)	148 (38.1)
Antidiabetic drug use, n (%)	209 (12.3)	143 (38.9)	63 (6.7)	3 (0.8)
Statin use, n (%)	158 (9.3)	95 (25.8)	59 (6.2)	4 (1.0)

Abbreviations: n, number of individuals; SD, standard deviation; kg, kilogram; m, meter;

*Diet score is composed based on consumptions of 5 food groups including fruits and vegetables, fish, whole grains, sugar-sweetened beverages, and sodium.

Table 2.

Association of cardiovascular health score with incident Alzheimer's dementia

Cardiovascular Health Score	N	Cases/PY	HR (95%CI)
Continuous			
Per 1-point increase	1702	351/14226.5	0.85 (0.77 – 0.94)
Categorical			
0–6	368	85/2770.8	1.00 (reference)
7–9	946	198/8174.9	0.45 (0.29 – 0.70)
10–14	388	68/3280.9	0.39 (0.23 – 0.68)

Abbreviations: PY, person years.

Models were adjusted by age, sex, race, education, APOE e4, cognitive activities, depression (CESD score), and cardiovascular disease (stroke and/or heart disease)

Table 3.

Association of cardiovascular health score with incident Alzheimer's dementia stratified by established risk factors

Cardiovascular Health Score (per 1-score increase)	N	Cases/PY	HR (95%CI)
Sex			
Men	653	138/5322.4	0.84 (0.7 – 1.00)
Women	1049	213/8904.1	0.85 (0.75 – 0.96)
Race			
Black or African Americans	906	218/7912.9	0.84 (0.74 – 0.96)
White	796	133/6313.7	0.84 (0.71 – 0.99)
Education			
<=12	887	225/7462.3	0.88 (0.77 – 1.00)
>12	815	126/6764.2	0.80 (0.68 – 0.94)
APOE e4 allele			
No	1162	204/9764.5	0.83 (0.72 – 0.95)
Yes	540	147/4462.1	0.87 (0.75 – 1.01)
Cardiovascular disease			
No	1428	285/12134.8	0.85 (0.76 – 0.96)
Yes	274	66/2091.7	0.81 (0.65 – 1.00)

Abbreviations: PY, person years; HR, hazard ratio; CI, confidence interval.

Models were adjusted by age, sex, race, education, APOE e4, cognitive activities, depression (CESD score), and cardiovascular disease (stroke and/or heart disease)

Table 4:

Association of cardiovascular health score with white matter hyperintensity, hippocampus, and gray matter volumes

Cardiovascular Health Score	N	Mean	Beta	95%CI
White matter hyperintensity				
Continuous				
Per 1-point increase	671	0.788	−0.028	−0.05, −0.005
Categorical				
0–6	140	0.871	0	reference
7–9	367	0.769	−0.134	−0.242, −0.026
10–14	164	0.757	−0.142	−0.272, −0.012
Hippocampus				
Continuous				
Per 1-point increase	671	0.692	0.001	−0.001, 0.003
Categorical				
0–6	140	0.69	0	reference
7–9	367	0.694	0.013	0.002, 0.024
10–14	164	0.69	0.01	−0.002, 0.023
Gray matter				
Continuous				
Per 1-point increase	671	2.549	0.002	0.001, 0.004
Categorical				
0–6	140	2.546	0	reference
7–9	367	2.548	0.007	0.002, 0.013
10–14	164	2.554	0.013	0.007, 0.02

White matter hyperintensities and hippocampal volumes were corrected for intracranial volume, multiplied by 1000, and log10-transformed to normalize the data. Means showed in the table are age-adjusted.

Regression models were adjusted by age, sex, race, education, and APOE e4, and time from cardiovascular health to MRI assessments.